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Journal of Agromedicine

ISSN: 1059-924X (Print) 1545-0813 (Online) Journal homepage: www.tandfonline.com/journals/wagr20

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To cite this article: Rietta S. Wagoner , Nicolas I López-Gálvez , Robert A. Canales , Paloma I. Beamer , Leslie V. Farland , Frank A. von Hippel , Jill G. de Zapien , Cecilia B. Rosales & Melissa A. Furlong (08 Jun 2026): Associations of Heat Exposure with Acute Kidney Injury and Kidney Function in Mexican Agricultural Workers, Journal of Agromedicine, DOI: 10.1080/1059924X.2026.2679282

To link to this article: https://doi.org/10.1080/1059924X.2026.2679282

Published online: 08 Jun 2026.

JOURNAL OF AGROMEDICINE
https://doi.org/10.1080/1059924X.2026.2679282

Associations of Heat Exposure with Acute Kidney Injury and Kidney Function in Mexican Agricultural Workers

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ABSTRACT

Objective: Agricultural workers endure physically demanding, high heat work daily, increasing the risk of kidney injury and reduced kidney function. However, few studies have examined individual measures of heat exposure and risk of kidney injury and impaired function. We assessed the association between measures of heat exposure with acute kidney injury and kidney functioning among agricultural workers, compared to a group of office workers in the same region.
Methods: We recruited 77 adult males working in agriculture and 21 adult males in office jobs in Sonora, Mexico in 2019. We administered a demographic questionnaire to participants. A proxy physiological strain index (PSI), based on point measurements of heart rate and tympanic temperature, was used to estimate individual heat exposure. Kidney function was measured using the estimated glomerular filtration rate (eGFR). Kidney injury was assessed via urinary neutrophil gelatinase-associated lipocalin (uNGAL). We compared uNGAL and eGFR over time in the two study groups. We assessed proxy PSI associations with uNGAL and eGFR using linear mixed-effects models, adjusting for age, body mass index, and urinary specific gravity factor.
Results: We observed statistically significant differences between agricultural and office workers for eGFR (GM: 121.85 vs. 115.66 mL/min/1.73 m^2, $p = .04$). Among agricultural workers, creatinine-adjusted uNGAL levels rose in summer compared to spring (GM: 4.47 vs. 1.98 mg/g creatinine, $p < .01$), and eGFR declined during the same period GM:(108.41 vs. 122.38 mL/min/1.73 m^2, $p < .01$). In mixed models, proxy PSI was inversely associated with eGFR (β-coefficient :-2.87, 95% CI: −4.02, −1.72).
Conclusion: Season and proxy PSI predicted kidney functioning in agricultural workers in this study. As climate warming continues, high-risk occupational groups such as agricultural workers will face increasing heat-related health risks.

KEYWORDS
Acute kidney injury; farmworker; heat stress; kidney function; uNGAL

Introduction

Climate change poses an increasing threat to agricultural populations in temperate and tropical regions; it is expected that rising global temperatures will continue to drive an increase in the number and intensity of extreme heat events.[1] The Intergovernmental Panel on Climate Change (IPCC) predicted an increase in adverse health impacts due to heat, including malnutrition and physical ailments.[1] Furthermore, climate change is expected to increasingly impact levels of occupational heat stress.[2]

Due to their adverse socioeconomic status,[3] migratory and seasonal agricultural workers are more likely to accept and remain in high-risk jobs, making them a vulnerable group.[4] In recent decades, populations of young outdoor laborers have experienced an excess of chronic kidney disease (CKD) unrelated to the established risk factors for CKD: older age, hypertension, and diabetes.[5–7] This phenomenon is referred to as chronic kidney disease of unknown etiology (CKDu), chronic kidney disease of unknown cause, and more recently, chronic kidney disease of non-traditional origin.[8] Factors such as heat stress/strain, repeated acute kidney injury, and dehydration are hypothesized to play a major role in this disease.[9–11] However, few studies have used individual measures of heat exposure in assessments of heat stress/strain and kidney complications.

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As an individual's core body temperature increases, work intensity is elevated, and/or extracellular volume is depleted, a cascade of adverse outcomes can occur. The physiological responses can include rhabdomyolysis, kidney hypoperfusion, hypokalemia, and acute kidney injury (AKI).[12,13] AKI is an abrupt decline in kidney functioning that is reversible with proper and timely treatment.[14] When renal functioning declines, the kidneys are less able to carry out normal blood-filtering processes, properly excrete wastes, correctly concentrate urine, and conserve critical electrolytes.[15] Individuals who experience AKI are more likely to develop CKD, which can progress to end-stage renal disease (ESRD), exacerbate existing CKD, and face an increased risk for non-kidney events such as myocardial infarction or stroke.[14] Urinary biomarkers are increasingly used to assess kidney injury and functioning, including neutrophil gelatinase-associated lipocalin (NGAL) and albumin.[6–19] NGAL, a small peptide belonging to the lipocalin family, is immediately upregulated as a response to renal injury with increases in urinary concentrations 10 to 100-fold in the first two hours following renal injury.[16,20]

Study objectives

In previous studies, our team highlighted agricultural workers' exposure to heat during the workday and heat effects on longer-term kidney function.[21] The objectives of the current study are to further assess AKI and kidney function over time, compare two exposure groups (i.e., agricultural workers and office workers), and assess associations between components of heat stress and AKI/kidney function.

Methods

Study design overview

While Sonora is not currently identified as an endemic region for CKDu, it has a large agricultural workforce that remains underrepresented in existing research. Our study was designed to address this gap by providing much-needed surveillance data for an underserved population. Grape workers in particular represent a sizable and economically important sector in Sonora, making them a relevant and valuable group for understanding potential occupational and environmental health risks. Biospecimens and questionnaires from a cohort of adult males working in agriculture and a group of adult male indoor office workers in northern Mexico were analyzed in this pilot study. Only men were recruited for the original cohort due to the overwhelming proportion of men working in this industry (95% men vs. <5% women).[22] Blood and urine samples were collected from the agricultural group during the spring (i.e., baseline) when they first arrived at the farm unacclimated and summer 2019 (i.e., follow-up). Baseline sampling took place in February 2019 through early March 2019 and follow-up from June 2019 through July 2019. Samples were collected once from office workers in March 2019.

Statement of IRB approval

All study protocols and written materials were approved by the University of Arizona Human Subjects Protection Program (IRB#1810987689 R001) before the study began.

Study population

We recruited 77 adult male workers from a commercial table grape farm in February 2019 in Sonora, Mexico, with the assistance of field supervisors and farm doctors. Similarly, 21 adult males working in office occupations were recruited from Hermosillo, Sonora in March 2019. Non-agricultural participants were eligible for inclusion if they were 18 years or older, were employed in an indoor occupation, and were not employed in agricultural work. Agricultural participants were eligible for inclusion in the study if they were 18 years or older and planned on working on the farm through July (i.e., for the duration of the grape harvest). All sampling procedures were explained in Spanish and written consent was obtained for inclusion in the study. Participants were compensated with a small monetary payment for their time.

Assessments

All agricultural worker assessments took place on a commercial grape farm during the workday, located approximately 30 km from the city of Hermosillo, while the office worker assessments took place in Hermosillo. Farm workers worked the same number of hours per day.

Questionnaires

At the conclusion of the workday, we orally administered a paper questionnaire in Spanish with the assistance of trained research staff. The questionnaire included questions regarding demographics, such as age, place of birth, education, preferred language, monthly income, smoking/drinking status, hypertension, renal issues, chronic diseases, painful urination, and NSAID usage. The questionnaires were later transcribed/entered electronically using encrypted REDCap software hosted at the University of Arizona.

Environmental assessments

Environmental conditions were measured and recorded to assess whether participants were working at or above recommendations set by the American Conference for Governmental Industrial Hygienists (ACGIH) Action Limit and Threshold Limit Value (TLV) for heat stress.[23] The Action Limit represents a more conservative threshold intended for unacclimatized workers, whereas the TLV reflects conditions considered acceptable for workers who are acclimated to the thermal environment and metabolic demands of the job.[23] During each sampling day, a continuously logging wet-bulb globe temperature (WBGT) monitor (Reed Instruments, Wilmington, NC, USA) was set to log at 1-minute intervals throughout the workday in a location approximately 500 meters from the fieldwork to collect data for agricultural participants and in the office building in Hermosillo to collect data for office participants. The WBGT meter was not moved during the shift. An 8-hour WBGT workday average was calculated for each worker. Briefly, the WBGT incorporates air temperature, the natural wet bulb temperature (i.e., the temperature of the air in relation to the relative humidity), and the globe temperature (i.e., a measure of radiant energy), as seen in Equation 1 for outdoor settings and Equation 2 for indoor settings,[24]

$$Outdoor\ WBGT = 0.7NWB + 0.2GT + 0.1DB \tag{1}$$

$$Indoor\ WBGT = 0.7NWB + 0.1DB \tag{2}$$

where WBGT is the wet bulb globe temperature index, NWB is the natural wet bulb temperature, GT is globe temperature, and DB is dry-bulb temperature.

Clothing type and layers were observed and assigned values according to the ACGIH Clothing Adjustment Factors for Some Clothing Ensembles.[25] The clothing adjustment factor was added to each worker's 8-hour WBGT to calculate the effective WBGT ($WBGT_{eff}$). Work tasks, working speed, use of tools, directional movement, and pushing/lifting activities were observed, recorded, and assigned respective metabolic rate estimates from the ACGIH Table for Metabolic Rate Categories and the Representative Metabolic Rate with Example Activities.[25] The $WBGT_{eff}$ and metabolic rate were then compared to the ACGIH Action Limit and TLV for heat stress. Due to a lack of inter-participant variability, $WBGT_{eff}$ was not included in statistical models.

Individual measures

As explained previously in Lopez-Galvez et al.[21] tympanic temperature was collected using a calibrated tympanic thermometer (Braun Thermoscan ExacTemp model IRT 6520, Braun, South Boston, MA, USA), and heart rate was recorded using a digital upper-arm sphygmomanometer (Omron M10-IT, Omron Healthcare Inc., Bannockburn, IL, USA). Measurements were obtained once during the work shift while workers briefly paused their work in the field. After the workday, participants visited the on-site clinic where body weight and height were recorded, and body mass index (BMI) was calculated. Tympanic temperature and heart rate were then measured again approximately 2–4 hours after the workday while participants were no longer engaged in work activities (post-work measurement). Physiological strain was estimated using the Physiological Strain Index (PSI) equation (Equation 6).[26] Because continuous measurements of core temperature and heart rate were not available, PSI values were calculated using single measurements of tympanic temperature and heart rate obtained during the workday and again after the workday. These values therefore represent an approximation of physiological strain derived from spot measurements rather than a full implementation of the original continuous PSI methodology, and will be referred to as "proxy PSI" throughout.

$$PSI = \frac{5(Temp\ work - Temp\ post - work)}{39.5 - Temp\ post - work} + \frac{5(HR\ work - HR\ post - work)}{180 - HR\ post - work} \quad (3)$$

where *Temp work* is the tympanic temperature recorded during the workday, *Temp post-work* is the tympanic temperature recorded after the workday (i.e., at rest), *HR work* is heart rate recorded during the workday, and *HR post-work* is heart rate recorded after the workday (i.e., at rest). PSI ranges from 0 to 10, with 0 representing no heat strain and 10 representing the highest level of heat strain.

Urine was collected twice for each participant: first-morning void urine samples were collected the morning after the observed workday in sterile 120 mL polyethylene plastic containers. A portion of urine was transported on ice to a local laboratory (Laboratorio Bio-Clinico Martinez, Hermosillo-Sonora, Mexico) to be processed. Remaining urine was transported within 6 hours of collection and stored at −80°C until analysis.

Laboratory analytical methods for biospecimen

Urinary specific gravity was analyzed using a digital hand-held refractometer (PAL-10S Specific Gravity Refractometer, Atago, China). A specific gravity factor (SGF) was calculated using Equation 6

$$Specific\ Gravity\ Factor = |(1.02 - (SG) - 1)| \quad (4)$$

where SG is urinary specific gravity.[27] SGF is a correction factor derived from the measured urine specific gravity to standardize biomarker concentrations to a reference hydration level.

Analysis of creatinine was done following the manufacturer's protocol (Parameter Creatinine Assay 2014 protocol, R&D Systems, Inc. Minneapolis, MN, USA). Urinary albumin was measured using a multi-parameter dipstick (Bayer Clinitek Chemistry Analyzer with Multistix 10SG reagent strips; Siemens Diagnostics, Pennsylvania, USA). The albumin-to-creatinine ratio was calculated by dividing albumin levels by creatinine levels. Urinary NGAL (uNGAL) concentrations were measured as a biomarker of kidney injury, rather than used to define acute kidney injury (AKI) based on a specific threshold. Analysis of uNGAL from baseline and follow-up was done per the manufacturer's protocol (Quantikine ELISA Human Lipocalin-2uNGAL Immunoassay 2018 protocol, R&D Systems, Inc. Minneapolis, MN, USA). Briefly urine samples were thawed to room temperature, centrifuged at 15,000 ×g for 10 minutes at 4°C, and supernatant was collected. The supernatant was diluted with Calibrator Diluent RD5-24 to ensure concentrations fell within the quantitative range of the standard curve and was analyzed in triplicate. Inter- and intra-assay coefficients of variation were below 12%, and the detection limit was < 0.15 ng/mL, based on a calculated limit of detection (LOD) of 0.121 ng/mL.

Laboratory analytical methods for blood samples

Blood samples were collected post workday via venipuncture by an on-site physician using 4 mL BD Vacutainer blood collection tubes and delivered on ice to a local laboratory (Laboratorio Bio-Clinico Martinez, Hermosillo-Sonora, Mexico) to be processed the same day as sample collection. Creatinine was analyzed using the VITROS CREA single-slide enzymatic method and uric acid was analyzed using the VITROS URIC slide method (VITROS, Ortho Clinical Diagnostics, Rochester, NY, USA). The serum creatinine and uric acid were completed using an automated VITROS 350 Chemistry Systems analyzer (Ortho Clinical Diagnostics, Rochester, NY, USA). Sodium, blood urea nitrogen (BUN), and glucose were measured using the Enzymatic 81 Method with a fully automated VITROS 350 chemistry system analyzer (VITROS Na, BUN, GLUC; Ortho Clinical Diagnostics, Rochester, NY, USA). Serum osmolality (mOsm/L) was calculated from sodium, blood urea nitrogen (BUN), and glucose using the standard equation:

$$2 \times [NA^{+}] + \frac{glucose}{18} + \frac{BUN}{2.8} \quad (5)$$

The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation modified by Stevens et al. [28] to include a four-level race variable (Black, Asian, Native American and Hispanic, and White and other) was used to estimate glomerular filtration rate (eGFR) for each timepoint, as seen in Equation 6 and Equation 6,[28]

$$For\ Serum\ Cr\ levels \leq 0.90,\ eGFR = 143\ x\ 0.993\ Age\ x(Serum\ Cr/0.9) - 0.412 \quad (6)$$

$$For\ Serum\ Cr\ levels > 0.90,\ eGFR = 143\ x\ 0.993\ Age\ x(Serum\ Cr/0.9) - 1.21 \quad (7)$$

where Serum Cr is serum creatinine and eGFR is the estimated glomerular filtration rate. We utilized the original CKD-EPI equation to maintain comparability with prior studies in similar populations, including those focused on Mesoamerican nephropathy, and because prior analyses of this dataset showed no meaningful differences when using the updated 2021 equation.

Data analysis

All urinary samples were analyzed in triplicate, and arithmetic mean concentrations for the biomarkers were used for each set of triplicate samples. All values below the LOD were substituted with the LOD/ √2. To account for urinary concentration levels, the uNGAL biomarker was adjusted by urinary creatinine levels (g/mL) and is presented as µg uNGAL/g urinary creatinine (µg/g) in the descriptive statistics. Data were assessed for normality using a Shapiro-Wilk test, visually using histograms and q-q plots, and via descriptive statistics. Arithmetic mean and standard deviation were calculated for normally distributed data while geometric mean and geometric standard deviation were calculated for non-normally distributed data. Baseline data for farmworkers were compared to follow-up levels using a paired t-test for normally distributed data and a Wilcoxon signed-rank test for non-normally distributed data. Baseline data for farmworkers were compared to non-farmworkers using Student's t-test for normally distributed data and Wilcoxon rank-sum/Mann Whitney U test for non-normally distributed data.[29]

To account for the repeated measures of exposures and outcomes, we used linear mixed-effects models with a random effect for participant, to evaluate associations of proxy PSI (exposure) with uNGAL and eGFR (kidney outcomes). In a second set of models, we added a time point covariate to evaluate if time was a statistically significant predictor of uNGAL, independent of heat strain, as measured by the proxy PSI. For uNGAL linear mixed-effect models, we included timepoints 1 (i.e., baseline) and 5 (i.e., final follow-up). In eGFR linear mixed-effect models, we included time points 1, 2, 3, 4, and 5. Finally, to evaluate whether proxy PSI was predictive of the longitudinal change in uNGAL and eGFR, we used linear regression models and changed the outcome to the change in uNGAL and eGFR from baseline to the timepoint 5 follow-up. All adjusted linear mixed effect and linear regression models included covariates that were selected *a priori*, including age, urinary SGF in uNGAL models, and BMI, based on evidence in the literature suggesting these variables may be important covariates for the relationships between environmental stressors and kidney outcomes [9,30]

Results

Demographics

All participants ($n = 77$ farmworkers and 21 non-farmworkers) were male; the mean age was similar for both groups, 29 and 31 years for farmworkers and non-farmworkers, respectively (Table 1). The two groups differed in their Mexican state of origin, primary language spoken, height, education level, monthly income,

Table 1. Participant demographics by occupation ($n = 98$), data from Sonora, Mexico, March 2019.

		Overall	Office Worker	Farmworker
		$n = 98$	$n = 21$ (21.4%)	$n = 77$ (78.6%)
Male	**n (%)**	98 (100%)	21 (100%)	77 (100%)
Age in years	**Mean (SD)**	29.62 (9.38)	31.24 (8.58)	29.18 (9.59)
State of origin	**n (%)**			
Sonora		16 (16.3%)	16 (76.2%)	0 (0.0%)
Puebla		43 (43.9%)	2 (9.5%)	41 (53.2%)
Chiapas		37 (37.8%)	2 (9.5%)	35 (45.5%)
Other		2 (2.0%)	1 (4.8%)	1 (1.3%)
Primary language spoken	**n(%)**			
Spanish		70 (71.4%)	20 (95.2%)	50 (64.9%)
Indigenous or Other		28 (28.6%)	1 (4.8%)	27 (35.1%)
Weight (kg)	**Mean(SD)**	74.26 (25.08)	88.04 (48.11)	70.49 (11.27)
Height (cm)	**Mean (SD)**	165.61 (8.72)	173.46 (12.02)	163.47 (6.11)
Body mass index (kg/m^2)	**Mean (SD)**	26.28 (4.00)	25.99 (4.93)	26.35 (3.74)
Education level	**n(%)**			
Less than high school		76 (77.6%)	4 (19.0%)	72 (93.5%)
Completed high school or higher		22 (23.7%)	17 (81.0%)	5 (6.9%)
Monthly income ($USD)	**n(%)**			
<$100		50 (53.8%)	0 (0.0%)	50 (69.4%)
$100–$200		19 (20.4%)	3 (14.3%)	16 (22.2%)
$200–$500		10 (10.8%)	5 (23.8%)	5 (6.9%)
$500–$1000		10 (10.8%)	9 (42.9%)	1 (1.4%)
>$1000		4 (4.3%)	4 (19.0%)	0 (0.0%)
Unknown		5 (5.1%)	0	5 (6.5%)
Smoking n(%)[a]	**n(%)**	57 (62.0%)	17 (81.0%)	40 (56.3%)
Alcohol consumption within previous 2 days[b]	**n(%)**	83 (89.2%)	13 (61.9%)	70 (97.2%)

[a]Six individuals declined to answer the question.
[b]Five individuals declined to answer the question.

and alcohol consumption. The majority of farmworkers migrated from the southern states of Puebla and Chiapas (53.2% and 45.5%), while 16 (76%) of non-farmworkers were from Sonora. A larger proportion of farmworkers spoke an Indigenous language as their primary language (35.1%) compared to the non-farmworker group (4.8%). Nearly all farmworkers had attained less than a high school degree (93.5%) whereas most non-farmworkers had completed high school or higher education (81%). Similarly, over half (69.4%) of farmworkers reported earning less than USD 100 per month whereas none of the non-farmworkers reported earning less than USD 100 per month.

Clinical measurements

We observed statistically significant differences between farmworkers and non-farmworkers for the following clinical measurements: serum urea, blood urea nitrogen, blood osmolality, plasma glucose levels, and eGFR (Table 2). The geometric mean eGFR at baseline for farmworkers was 121.85 (geometric standard deviation: 1.1 mL/min/1.73 m^2) and for non-farmworkers was 115.66 (geometric standard deviation: 1.12; mL/min/1.73 m^2; Table 2). Similarly, we observed statistically significant differences between farmworkers at baseline and follow-up for the following clinical measurements: serum urea, blood urea nitrogen, blood uric acid, blood urea nitrogen:serum creatinine ratio, serum creatinine, plasma glucose levels, urinary albumin, eGFR, and uNGAL (Table 2). The uNGAL geometric mean for non-farmworkers was 3.75 ng/mL (geometric standard deviation: 3.44), whereas for farmworkers at baseline it was 2.77 ng/mL (geometric standard deviation: 2.54) and for farmworkers at follow-up it was 7.19 ng/mL (geometric standard deviation: 2.59; Table 2). Additionally, SGF-adjusted uNGAL for farmworkers at baseline was statistically significantly different than at follow-up ($p < .01$; Table 2). At baseline, 19% of the farmworkers had hypertension compared to just 5% of office workers and 11% of farmworkers had

Table 2. Farmworker (FW) and office worker clinical data, by occupation and timepoint. Data from Sonora, Mexico 2019.

Variable[a]		Overall	FW Baseline	FW Follow-up	Office	Office Vs FW Baseline *p*-value[b]	FW Baseline Vs FW Follow-Up *p*-value[c]
	Mean (±SD)	n = 98	n = 77	n = 77	n = 21		
Serum urea (mg/dL)		27.79 (6.41)	26.05 (5.66)	28.30 (6.57)	32.46 (6.05)	**<0.01**	**<0.01**
Blood urea nitrogen (mg/dL)		13.01 (2.88)	12.27 (2.66)	13.43 (3.10)	14.30 (2.15)	**<0.01**	**<0.01**
Blood uric acid (mg/dL)		5.76 (1.15)	5.58 (1.14)	5.94 (1.20)	5.79 (0.89)	0.39	**0.01**
Blood urea nitrogen: serum creatinine ratio		15.93 (3.84)	16.39 (3.79)	14.82 (3.66)	17.86 (3.70)	0.12	**<0.01**
	Geomean (±GSD)						
Serum creatinine (mg/dL)		0.82 (1.22)	0.75 (1.18)	0.91 (1.22)	0.81 (1.19)	0.09	**<0.01**
Serum sodium (mmol/L)		140.53 (1.03)	139.91 (1.04)	141.74 (1.02)	138.82 (1.04)	0.05	0.05
Blood osmolality (mmol/kg)		268.57 (1.04)	268.95 (1.04)	272.03 (1.02)	256 (1.06)	**<0.01**	0.19
Plasma glucose levels (mg/dL)		65.99 (1.37)	75.01 (1.33)	61.87 (1.28)	51.14 (1.51)	**<0.01**	**<0.01**
Urinary specific gravity		1.02 (1.01)	1.02 (1.01)	1.02 (1.01)	1.02 (1.01)	0.81	0.26
Urinary albumin (mg/L)		16.84 (2.03)	24.04 (2.24)	11.62 (1.46)	16.87 (1.75)	0.08	**<0.01**
Estimated glomerular filtration rate (mL/min/1.73 m^2) *		114.5 (1.18)	121.85 (1.10)	106.59 (1.22)	115.66 (1.12)	**0.04**	**<0.01**
uNGAL (ng/mL)		4.35 (2.93)	2.77 (2.54)	7.19 (2.59)	3.75 (3.44)	0.20	**<0.01**
Creatinine-adjusted uNGAL (mg/g creatinine)		2.94 (2.75)	1.98 (2.63)	4.47 (2.2)	2.76 (3.69)	0.14	**<0.01**
Hypertension[d]	**n(%)**					0.92	0.92
No		135 (80.8%)	57 (79.2%)	60 (81.1%)	18 (85.7%)		
Yes		28 (16.8%)	14 (19.4%)	13 (17.6%)	1 (4.8%)		
Unsure		4 (2.4%)	1 (1.4%)	1 (1.4%)	2 (9.5%)		
Did not answer		8 (4.6%)	5 (6.5%)	3 (3.9%)	0		
Renal Issues[d]	**n(%)**					0.24	0.95
No		139 (83.2%)	58 (80.6%)	61 (82.4%)	20 (95.2%)		
Yes		15 (9.0%)	8 (11.1%)	7 (9.5%)	0 (0.0%)		
Unsure		13 (7.8%)	6 (8.3%)	6 (8.1%)	1 (4.8%)		
Did not answer		8 (4.6%)	5 6.5%)	3 (3.9%)	0		
Chronic Diseases[d]	**n(%)**					0.65	1.00
No		160 (95.8%)	69 (95.8%)	71 (95.9%)	20 (95.2%)		
Yes		5 (3.0%)	2 (2.8%)	2 (2.7%)	1 (4.8%)		
Unsure		2 (1.2%)	1 (1.4%)	1 (1.4%)	0 (0.0%)		
Did not answer		8 (4.6%)	5 6.5%)	3 (3.9%)	0		
Painful urination[d]	**n(%)**					0.45	0.08
No		147 (91.3%)	62 (86.1%)	68 (95.8%)	17 (94.4%)		
Yes		14 (8.7%)	10 (13.9%)	3 (4.2%)	1 (5.6%)		
Did not answer		14 (8%)	5 6.5%)	6 (7.8%)	3 (14.3%)		
NSAID usage[d]	**n(%)**					0.68	**<0.01**
No		127 (78.9%)	64 (88.9%)	46 (64.8%)	17 (94.4%)		
Yes		34 (21.1%)	8 (11.1%)	25 (35.2%)	1 (5.6%)		
Did not answer		14 (8%)	5 6.5%)	6 (7.8%)	3 (14.3%)		

Abbreviations: uNGAL, neutrophil gelatinase associated lipocalin; NSAIDS, non-steroidal anti-inflammatory.
Farmworker baseline: February and March 2019; Farmworker follow-up : June and July 2019; Office workers: March 2019.
[a]Seven farmworkers were missing clinical data.
[b]A Wilcoxon Rank Sum Test was used for non-normally distributed data to compare farmworker to non-farmworker baseline.
[c]A Wilcoxon Two Sample Test (i.e., Signed Rank) was used for non-normally distributed data to compare farmworker baseline and follow-up.
[d]A Fisher Test (between categorical variables).
* Follow-up represents timepoint 5 for eGFR.

reported kidney issues compared to 0 office workers (Table 2). Finally, 89% of farmworkers reported NSAID usage at baseline compared to 65% at follow-up.

Heat exposure: WBGT and proxy PSI

Heat stress was higher during the follow-up sampling period than during the baseline sampling period. For the baseline data collection period (i.e., spring month), the $WBGT_{eff}$ for all farmworkers ranged from less than 20°C to 28°C, and the metabolic rate ranged from less than 180 watts (W) to over 400W, reaching and surpassing the ACGIH Action Limit and TLV (Figure 1). The air temperature ranged from 20.5°C to 24°C, the globe temperature ranged from 20.8°C to 24.2°C, the wet-bulb temperature ranged from 10.2°C to 13.1°C, and work took place outside in shaded and partial direct sun throughout the day. Work tasks in the spring included trimming and shaping grape plants and workers were observed running between rows of plants.

During the follow-up data collection period (i.e., summer month), the $WBGT_{eff}$ for all farmworkers ranged from 28°C to 34°C, and the metabolic rate ranged from less than 100W to over 300W, reaching and surpassing the ACGIH Action Limit and TLV. The air temperature ranged from 33.2°C to 37.7°C, the globe temperature ranged from 36.4°C to 41.5°C, the wet-bulb temperature ranged from 20.6°C to 22.6°C, and work took place outdoors in zero, partial, and full shade throughout the day as workers moved through and between rows of mature grape vines. Work tasks included: clipping mature grape bunches, packaging and weighing grapes, and carrying and loading boxes of grapes to a nearby truck. The proxy PSI of farmworkers at baseline (median: 2.39) was significantly different from that of office workers (median: 1.78, $p < .01$). A similar pattern was observed at follow up (medians: 2.39 in spring versus 4.08 in summer, $p < .01$; Figure 2).

Repeated measure associations between proxy PSI and kidney outcomes

uNGAL: Among farmworkers, we observed positive associations between proxy PSI (0.37, 95% CI: 0.23, 0.51), post-work heart rate (0.03, 95% CI: 0.00, 0.05), working heart rate (0.02, 95%CI: 0.01, 0.03), post-work tympanic temperature (0.08, 95% CI: 0.00, 0.17), and working tympanic temperature (0.95, 95% CI: 0.55, 1.36) and uNGAL in multivariable models controlling for age and BMI (Table 3). To help interpret these beta coefficients, each value reflects the estimated change in uNGAL associated with a one-unit increase in the corresponding physiological measure; for example, a one-unit increase in proxy PSI was associated with a 0.37 mg increase in uNGAL.

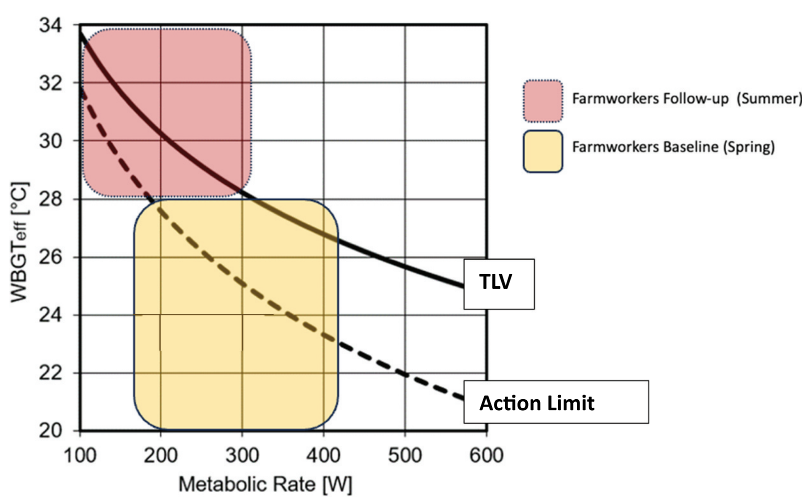

Figure 1. 8-hour wet-bulb globe temperatures by sampling period overlaid onto the American Conference for Governmental Hygienists threshold Limit value (TLV) Figure for heat stress. Summer months represent July 2019 and Spring months represent March 2019. The dashed line represents the Action Limit and the solid line represents the TLV.

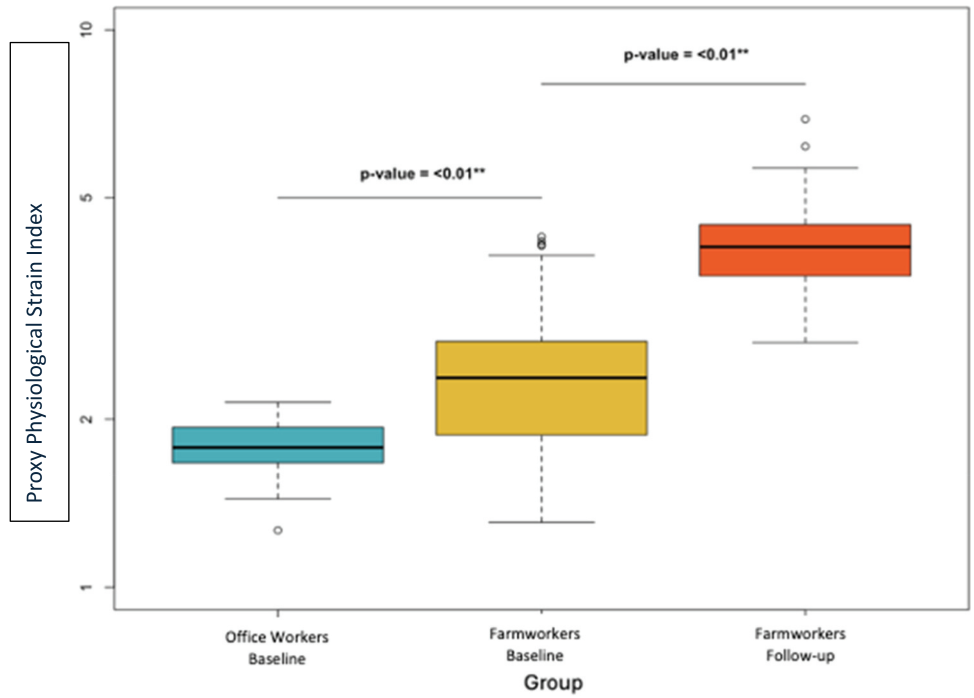

Figure 2. Box plot of proxy physiological strain index (PSI) by group. PSI is a unitless scale from 1–10, with 1 indicating no physiological strain and 10 indicating highest physiological strain. A two-sided Wilcoxon rank-sum/mann Whitney U test was used to compare proxy PSI in farmworkers vs. non-farmworkers at time point 1. A two-sided paired Wilcoxon signed-rank test was used to compare proxy PSI between farmworkers at baseline and follow-up.

eGFR: Similarly, we observed negative associations between proxy PSI (−2.87, 95% CI: −4.02, −1.72), post-work heart rate (−0.02, 95% CI: −0.15, 0.10), working heart rate (−0.17, 95% CI: −0.23, −0.10), post-work tympanic temperature (−0.23, 95% CI: −1.10, 0.65), and working tympanic temperature (−5.21, 95% CI: −8.11, −2.30) and eGFR in farmworkers after controlling for age and BMI (Table 4). The change in eGFR from baseline to follow-up was inversely associated with post-work heart rate (−0.25, 95% CI: −0.47, −0.03) and working heart rate (−0.59, 95%CI: −0.81, −0.37) measured at baseline (Table 4).

Table 3. Associations between proxy physiological strain index (PSI) and urinary neutrophil gelatinase-associated lipocalin (uNGAL) in a cohort of migratory farmworkers in Sonora Mexico in 2019 ($n = 77$, two timepoints).

	Outcome	
Predictor	uNGAL[a] b-Coefficient (95% CI)	ΔuNGAL[b] b-Coefficient (95% CI)
Proxy PSI	**0.37 (0.23, 0.51)**	1.04 (−4.02, 6.11)
Post-work heart rate (BPM)	**0.03 (0.00, 0.05)**	0.15 (−0.10, 0.40)
Working heart rate(BPM)	**0.02 (0.01, 0.03)**	0.05 (−0.18, 0.29)
Post-work tympanic temperature (°C)	**0.08 (0.00, 0.17)**	3.29 (−1.27, 7.84)
Working tympanic temperature (°C)	**0.95 (0.55, 1.36)**	3.79 (−2.70, 10.27)

Abbreviations and symbols: BPM, beats per minute; Δ, difference between baseline and follow-up.
Note: Higher uNGAL indicates more kidney injury.
All models include the following covariates: specific gravity factor, age in years, and body mass index (BMI).
[a]Linear mixed effect regression models were used to assess associations between urinary NGAL and each predictor variable with participant ID as the random effect.
[b]Linear regression models were used to assess whether the change in urinary NGAL was associated with the predictor variable at baseline.
Number of observations (N Obs.) for all models = 152.
Bolded values indicate statistical significance.

Table 4. Associations between proxy physiological strain index (PSI) and estimated glomerular filtration rate (eGFR) in a cohort of migratory farmworkers in Sonora Mexico in 2019 ($n = 77$, five timepoints).

	Outcome	
Predictor	eGFR[a] b-Coefficient (95% CI)	ΔeGFR[b] b-Coefficient (95% CI)
Proxy PSI	**-2.87 (−4.02, −1.72)**	−1.11(−6.85, 4.62)
Post-work heart rate (BPM)	−0.02 (−0.15, 0.10)	**-0.25 (−0.47, −0.03)**
Working heart rate(BPM)	**-0.17 (−0.23, −0.10)**	**-0.59 (−0.81, −0.37)**
Post-work tympanic temperature (°C)	−0.23 (−1.10, 0.65)	−0.63(−4.54, 3.27)
Working tympanic temperature (°C)	**-5.21 (−8.11, −2.30)**	2.98(−3.45, 9.40)

Abbreviations and symbols: BPM, beats per minute; Δ, difference between baseline and follow-up.
Note: Lower eGFR indicates reduced kidney function.
All models include the following covariates: age in years and body mass index (BMI).
[a]Linear mixed effect regression models were used to assess associations between eGFR and predictor, with participant ID as the random effect.
[b]Linear regression models were used to assess whether the change in eGFR was associated with the predictor variable at baseline.
Number of observations (N Obs.) for linear mixed effect regression models = 453 and for linear regression models = 114.
Bolded values indicate statistical significance.

Discussion

Overview

This study assessed kidney injury and heat exposure in a group of agricultural workers in Sonora, Mexico, compared these levels over time, and compared metrics to a group of office workers living and working in the same area. The effective WBGT for farmworkers met and surpassed both the ACGIH Action Level and TLV in the spring and summer and was much higher in the summer than in the spring months (Figure 1). The proxy PSI for farmworkers in the spring was significantly different from non-farmworkers, and the proxy PSI of farmworkers increased as the seasons progressed from spring to summer (Figure 2). Individual proxy PSI measurements were also associated with reduced kidney functioning as measured by eGFR. Together, these findings are consistent with established mechanisms of heat-related kidney injury, in which heat strain and dehydration lead to reduced renal perfusion, increased osmotic stress, and early tubular injury. Thus, our results suggest heat stress may contribute to early decreases in kidney health in agricultural workers.

Demographics, heat stress, and clinical biomarkers

The educational levels, income, and migration findings are similar to our previous observations of agricultural workers in Sonora, Mexico [31] and to those reported in the 2009 Encuesta Nacional de Jornaleros (National Agricultural Workers Survey) conducted by the Mexican federal governmental organization, Social Development Assistance Program for Agricultural Day Laborers, as well as in a Sonora-specific survey conducted by local researchers.[32,33]

The high metabolic rate observed in spring may be explained by the practice of workers running between lines, as they are paid by the number of lines completed per day. It is recommended that employers move away from this type of compensation, as it compromises worker health and safety; previous studies in agricultural populations have illustrated that workers make self-care decisions based on payment type, such that piece work/line payment can result in dehydration, over-exertion, and increased core body temperature.[34–37] Additionally, implementation of heat prevention training and protocols are an effective way to protect all workers from heat exposure. NSAID use among agricultural workers is an important contextual factor to note, given evidence that NSAID use during strenuous labor or heat stress may increase susceptibility to kidney injury.[38] The discrepancy between participants' reports of "chronic disease" and their responses to specific questions about hypertension or renal issues may reflect differences in how these terms were understood, including varying familiarity with medical terminology or prior clinical diagnosis. Most biomarker values for farmworkers and office workers fell within typical clinical reference ranges, suggesting observed differences were not clinically abnormal but may still reflect physiologic responses to heat exposure, dehydration, and seasonal workload. Notably, serum urea was above the upper clinical range across all groups, and farmworkers experienced small but meaningful increases in creatinine, urea, uric acid, and uNGAL over the season, consistent with transient renal stress. Although these changes are not diagnostic of acute kidney injury, their patterns align with biomarker shifts documented in heat-exposed populations and support the need for continued monitoring.[9]

Kidney injury: uNGAL

Several U.S. studies have also explored the connection between AKI and heat stress. A study of 283 agricultural workers in California observed a 12% incidence of AKI during a work shift, with increased odds of kidney injury among those who experienced heat strain.[39] Similarly, a study of 192 agricultural workers in Florida over multiple days reported a 33% incidence of AKI, and for every 2.8°C rise in the heat index, the odds of AKI increased by 37%.[30] Notably, both studies relied on serum creatinine – based criteria to define AKI, which differs from our use of uNGAL as an early marker of tubular stress and limits direct comparison across studies.

Several recent studies of agricultural populations have included urinary uNGAL as a biomarker of kidney functioning, with increased concentrations over time and higher levels in agricultural workers than in control populations.[40–42] The increase in creatinine-adjusted uNGAL observed in our study is similar to the increases seen in uNGAL levels in a cohort of sugarcane workers in Nicaragua, where the creatinine-adjusted geometric means of the cohort increased from 7.6 μg/g to 19.4 μg/g from pre-harvest baseline to end of harvest follow up.[40] Similarly, in another study in Nicaragua, an increase in uNGAL was observed in a cohort of sugarcane cutters at three-time points, with the median levels of creatinine-adjusted uNGAL increasing from 9.3 μg/g pre-shift on the first day of harvest to 17 μg/g at the follow-up in January 2013.[43] Our results are also similar to those observed in two Sri Lankan agricultural communities, with arithmetic means of 2.46 and 6.95 μg/g creatinine.[42] However, the levels of unadjusted uNGAL in this study were lower than those reported in a cohort of Guatemalan sugarcane workers, with arithmetic means ranging from 7.1 to 27.1 ng/mL urine.[44] The uNGAL levels observed in the non-farmworker group in our study are comparable to control populations in the aforementioned studies.

Kidney function: eGFR

The slightly higher baseline eGFR observed in farmworkers may be attributable to conditions preceding their arrival at the farm, such as prior environmental or occupational exposures, differences in environmental conditions for individuals migrating from southern Mexico, dehydration, or other individual-level factors that influence kidney function. Several Central American agricultural worker studies have also documented a decline in kidney function over the agricultural season. Although a gradual decrease in eGFR is expected with increasing age, the magnitude and rapidity of decline reported in these studies suggests changes beyond what would be attributable to aging alone. For example, in a cohort of 284 Nicaraguan sugarcane workers, workers had a reduction of at least 5.0 ml/min/1.73 m^2 over 6 months and workers with the largest increases in uNGAL over time had an average decline in eGFR of 4.6 ml/min/1.73 m.[40,45] Several agricultural health studies have reported a rise in serum creatinine levels across work shifts, with associations between reduced kidney function and elevated heat stress and/or dehydration.[30,46,47] A study of 189 sugarcane cutters in El Salvador found an increase in serum creatinine during the work shift, with a positive correlation with both temperature and heat strain.[46] Mix et al.[30] reported a change in eGFR from 112.8 to 102.5 mL/min/1.73 m^2 over a work shift in a group of 192 agricultural workers in Florida, and the percentage of individuals with eGFR below 90 mL/min/1.73 m^2 increased from

5% to 25% from pre-shift to post-shift. Additionally, findings from a Nicaraguan study demonstrated outdoor and agricultural work, as well as limited access to shade during the workday, were associated with a rapid decline in eGFR over a 2-year period.[47] Employment duration may also be affected by kidney health. In a study of over 4,000 Guatemalan sugarcane cutters, individuals who had reduced eGFR over time were more likely to leave employment (Hazard Ratio: 2.92, 95% CI: 1.88, 4.32).[48]

Strengths

This study had several important strengths, including the ability to follow a migratory agricultural population within Mexico. Another strength of this study is that all farmworker participants worked at the same farm, ate employer-provided meals together, and lived in communal on-site housing, resulting in relatively uniform occupational and environmental conditions. This reduced heterogeneity in true heat exposures and contextual factors that can influence physiological strain. In addition, we incorporated individualized proxy heat-exposure measurements (HR, tympanic temperature, and proxy PSI), which improved exposure assessment, although we acknowledge that these point measures may still include some degree of measurement error. The point measurements of heart rate and tympanic temperature used in this study represent proxy measures of heat exposure and may be subject to variability; future studies using continuous physiological monitoring and full PSI calculation are needed to validate these approaches. We were able to include a relatively novel biomarker to estimate AKI, adding to a growing body of evidence that early detection of kidney damage in agricultural workers is needed.

Limitations

This study has several limitations. We evaluated kidney function, heat exposure, and dehydration in a relatively small sample of male agricultural workers in a limited geographical setting, which restricts generalizability. With only two sampling time points for the agricultural workers, environmental variability was lower than what farmworkers typically experience. Similarly, because office workers were sampled at only one time point, we were unable to characterize the full range of their daily environmental exposures, which may differ from those of agricultural workers and introduce additional variability into between-group comparisons. Heart rate was measured in the field using an automated digital monitor that provides point measurements rather than continuous recording. Field conditions, including participant movement and the demands of ongoing work activities, may introduce variability in spot measurements. Consequently, heart rate values may be less precise than those obtained using devices that continuously record heart rate. Future studies should employ wearable sensors that track heart rate, skin temperature, and globe temperature to better assess heat exposure, which may strengthen associations by reducing nondifferential misclassification. WBGT was calculated from portable weather stations in fields and offices, but did not capture individual-level variation in sun exposure or indoor time, possibly misestimating heat exposure. Additionally, we estimated metabolic load in the WBGT calculation, which may underestimate heat strain; future studies should consider individualized metabolic load using accelerometers or similar tools. Further, for the proxy PSI calculation, we used tympanic (inner ear) temperature rather than rectal temperature to ensure that sample collection was feasible in field settings and acceptable to participants. Although rectal temperature is considered the gold standard for assessing core body temperature, tympanic measurements can be influenced by technique, cerumen buildup, probe positioning, and individual anatomical differences in the ear canal. As a result, tympanic temperature may underestimate or overestimate true core temperature, potentially introducing measurement error into the proxy PSI estimates. Additionally, the PSI calculation relies on baseline temperature and heart rate measurements that ideally should be collected immediately before work begins. In our study, these "post-work" values were measured 2–4 hours after the workday ended due to logistical constraints, and the timing was not uniform across participants. Because individuals recover at different rates, this variability may have introduced differential error in baseline values and, consequently, in the proxy PSI estimates. As a result, some proxy PSI values may underestimate or overestimate true physiological strain. We were unable to measure factors such as water intake, job demands, and detailed medical history, which may influence physiologic strain and kidney biomarkers. Although these were not confounders in our models, they represent unmeasured sources of variability that could affect interpretation of the results. We did not collect paired pre- and post-shift biological samples, such as blood, which would have allowed us to calculate changes in serum creatinine, an alternative indicator of acute kidney injury. Similarly, our assessment of kidney function relied on serum creatinine, which can increase due to muscle breakdown following strenuous physical labor. As a result, creatinine levels measured in a population engaged in physically demanding work may partially reflect muscle activity rather than true changes in kidney function. Although we were unable to calculate urinary albumin – creatinine ratios (UACR), future studies should incorporate this clinically informative measure to better characterize early kidney injury. Additionally, we interpreted uNGAL as a continuous biomarker of renal tubular injury, as the establishment of clinical thresholds for defining subclinical or clinical kidney injury are underway by the Kidney Disease Improving Global Outcomes (KDIGO) working group's KDIGO 2026 Clinical Practice Guideline for Acute Kidney Injury (AKI) and Acute Kidney Disease (AKD) March 2026 Draft. In addition, short-term intra-individual variability remains incompletely understood. While we observed within-group changes over time, the clinical significance of these changes is uncertain. Finally, the CKD-EPI formula has not been validated in this population.

Conclusions

This study builds on prior research linking heat stress and kidney damage by incorporating personal heat exposure measures among migratory Mexican farmworkers. Future work should aim to establish clinical thresholds for uNGAL and other AKI biomarkers to improve diagnostic accuracy. Surveillance of kidney function in farmworkers will require collaboration across health centers, clinics, academic institutions, public health agencies, and international organizations. On farms with medical staff, heat prevention and recovery efforts should accompany kidney injury surveillance, and employee housing should support post-work recovery.

Research should also explore other occupational and environmental nephrotoxic exposures, including metals, metalloids, and pesticides, and their possible combined effects. We recommend early clinical screening and intervention studies using the industrial hygiene hierarchy of controls to address hydration and reduce heat strain, including assessments of barriers to implementation.[19] Longitudinal studies, though challenging, are essential for understanding long-term effects of repeated AKI and should be coupled with prevention strategies outside the workplace, such as home cooling interventions and health education to empower farmworkers in protecting their kidney health.

Acknowledgments

We would like to thank the farmworkers who participated in this study. We would also like to thank the following individuals for their assistance in recruitment and collection/processing of samples: Dr. Juan Alday, Dra. Daniella Meyers, Fernanda Garavita, Marvin Chaires, Veronica Lugo, Gabriel Torres, Carolina Quijada, Marisol Verdugo, and Shawn Beitel. We would also like to thank Isaiah Casarez for assistance with statistical analysis and database support.

Author contributions

CRediT: **Rietta S. Wagoner:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Validation, Visualization, Writing – original draft; **Nicolas I López-Gálvez:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Writing – review & editing; **Robert A. Canales:** Conceptualization, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Software, Supervision, Writing – review & editing; **Paloma I. Beamer:**

Conceptualization, Funding acquisition, Investigation, Project administration, Resources, Supervision, Writing – review & editing; **Leslie V. Farland:** Formal analysis, Methodology, Supervision, Writing – review & editing; **Frank A. von Hippel:** Formal analysis, Methodology, Supervision, Writing – review & editing; **Jill G. de Zapien:** Conceptualization, Funding acquisition, Project administration, Supervision, Writing – review & editing; **Cecilia B. Rosales:** Conceptualization, Funding acquisition, Investigation, Project administration, Supervision, Writing – review & editing; **Melissa A. Furlong:** Data curation, Formal analysis, Funding acquisition, Methodology, Project administration, Software, Supervision, Validation, Visualization, Writing – review & editing.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

The work was supported by the University of Arizona Southwest Environmental Health Sciences Center [P30 ES006694, T32 ES007091]; Southern California NIOSH Education and Research Center Pilot Project Program [T42OH008412]; Southwest Center on Resilience for Climate Change and Health [P20ES036112-01]; Agricola Pozo Manuel University of Utah NIOSH Rocky Mountain Center for Occupational and Environmental Health Pilot/ Small Research Project Funding Program [T42OH00841418]; American Industrial Hygiene Association Arizona Chapter Student Research Funds University of Arizona Mel and Enid Zuckerman College of Public Health Dean's Student Research Fund University of California Davis NIOSH Western Center for Agricultural Health and Safety Small Grant Program [U54OH007550].

Data sharing

The data and computing code are available from the author upon reasonable request.

Ethical approval

All study protocols and written materials were approved by the University of Arizona Human Subjects Protection Program (IRB#1810987689R001) before the study began.

Generative artificial intelligence

During the preparation of this work the author(s) used OpenAI ChatGPT in order to improve readability and language of the manuscript. After using this tool/service, the author(s) reviewed and edited the content as needed and take(s) full responsibility for the content of the published article.

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