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Electrolyte Beverage Intake to Promote Hydration and Maintain Kidney Function in Guatemalan Sugarcane Workers Laboring in Hot Conditions

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Objectives: To evaluate impact of electrolyte supplementation on hydration status and health outcomes in Guatemalan agricultural workers performing heavy work under hot climatic conditions. **Methods:** A 3-week pragmatic trial was conducted with a group of 50 workers during the 2017 to 2018 sugarcane harvest. Workers received an electrolyte hydration intervention during 2 of the 3 weeks. Blood and urine samples were collected each week. **Results:** Increased electrolyte intake resulted in less muscle injury. Kidney function was maintained across the intervention period. Workers were adequately hydrated and average electrolyte levels remained in normal ranges. Mild indications of hyponatremia occurred at higher levels of fluid

intake. **Conclusions:** This trial demonstrates the feasibility of maintaining workers' electrolyte levels under extremely hot and humid conditions while mitigating muscle injury. Electrolyte supplementation should be added to standard workplace water, rest, and shade interventions to protect workers.

Keywords: agricultural workers, electrolyte intervention, hydration, international occupational health, kidney injury

With rising global temperatures, outdoor agricultural laborers are increasingly exposed to heat and high humidity for extended periods.^{1,2} Additionally, agricultural jobs can be extremely physically demanding, such as in manual sugarcane cutting, and are often performed in very hot, humid weather, especially in Latin America.^{3–6} Sugarcane workers can spend over 8 hours a day cutting and stacking on average 6 tons of cane.⁷ The high intensity of labor coupled with extreme climate put agricultural workers at increased risk of dehydration and hypohydration, defined as a state of decreased body water of 2% of body mass change due to sweat loss. Performing physical activity while losing body water impairs the body's ability to dissipate heat, increasing the risk for heat-related illness and injury,^{1,2,8–12} rhabdomyolysis, and exercise-associated hyponatremia, conditions that are commonly seen among endurance athletes.^{13–16} Additionally, acute kidney injury is one complication that is associated with exertional rhabdomyolysis^{17,18} which can lead to kidney failure if left untreated.^{19,20} Little is known of these health conditions in the occupational setting among workers who may experience these work conditions daily.

Electrolyte intake during endurance activities is important for preventing hyponatremia and maintaining euhydration. During prolonged exercise in the heat, losses of water, sodium, chloride, and potassium through sweat can be substantial.²¹ Current recommendations from the Occupational Safety and Health Administration (OSHA) and National Institute for Occupational Safety and Health (NIOSH) focus heat illness prevention guidelines mainly on plain water and rest.^{22,23} The OSHA "Water. Rest. Shade." guidance recommends water consumption but does not comment on electrolyte replacement.²⁴ Guidelines from NIOSH state, "Workers in heat <2 hours and involved in moderate work activities should drink 1 cup (8 oz.) of water every 15–20 minutes, but during prolonged sweating lasting several hours, they should drink sports drinks containing balanced electrolytes."²⁵ The recommended quantity of electrolytes is not specified; however, the guidelines acknowledge a need for further epidemiologic research to determine the appropriate electrolyte and water regimen for long-term work in the heat. Additionally, the concentration of electrolytes in standard sports drinks is much lower than that which is lost on average from sweat, making real-time electrolyte replacement with these drinks impossible without putting the individual at risk of hyponatremia.²⁵ Therefore, specific prescribing of water and electrolytes is necessary for those at risk of hypohydration and hyponatremia.²⁶

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Ethical Considerations: This study was approved by the Colorado Multiple Institutional Review Board (COMIRB) of the University of Colorado (#18-0957). De-identified data were provided to the Center for Health, Work & Environment by Pantaleon for this analysis; therefore, individual informed consent was not obtained.

The authors disclose no conflicts of interest.

Clinical significance: Agricultural workers perform intense physical labor in hot, humid conditions, placing them at risk for conditions including heat-related illness, hyponatremia, rhabdomyolysis, and kidney injury. Increased consumption of electrolyte solution can help mitigate muscle injury while preserving electrolyte balance and kidney function.

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A recent study in Guatemala found that a concerning proportion of sugarcane workers were consuming large quantities of plain water on average (15 L) and relatively low amounts of electrolyte solution (3 L) resulting in low serum sodium and potassium levels and putting them at risk for hyponatremia and hypokalemia.^{27,28} One potential behavioral intervention is the substitution of plain water with electrolyte beverages during the workday. Previous studies have shown this to potentially be protective against kidney injury, however the effects on hyponatremia are unknown.^{27,29,30} Since most of the existing evidence on fluid replacement has come from research on athletes, this study seeks to evaluate three different electrolyte and water regimens and the impacts on the health of sugarcane cutters—workers who are on the frontline of heat, humidity, and intense labor. Furthermore, we are not aware of any other studies that evaluate the efficacy and feasibility of electrolyte supplementation in an occupational field setting under hot conditions.

The goal of this pragmatic comparative effectiveness trial^{31,32} was to compare the different amounts of electrolyte supplementation and measure the effects on several health outcomes during typical work shifts of sugarcane workers. We hypothesized that increasing electrolyte solution intake would maintain hydration, reduce kidney and muscle damage, and mitigate other adverse health outcomes associated with physical labor in the heat, while maintaining overall productivity.

METHODS

Study Population

For this trial, a work group of male sugarcane cutters from the same community was selected using random sampling from a list of 46 active sugarcane cutter work groups employed at Pantaleon, an international agribusiness based in Guatemala. All participants were at least 18 years of age, were men, were screened for employment in November 2017, started the season with an estimated glomerular filtration rate (eGFR) of more than or equal to 90 mL/min/1.73 m² and had no major illnesses that might affect their ability to work. The group worked on plantations located within the boundaries of the Pantaleon sugar mill near Escuintla, Guatemala, and was living together in dormitory housing on company property. Sugarcane cutters at the company work a 6-day workweek followed by 1 day off and are paid a base wage that is in addition to compensation for the amount of cane they cut each week. Cane cutters work in the fields for approximately 8 hours per day with 2 hours of rest (three 20-minute breaks plus 1 hour for lunch). See Butler-Dawson et al³

for additional information regarding the field setting, population, and work practices.

Study Design

The effectiveness trial was conducted during 3 consecutive weeks in January 2018, approximately half-way through the harvest season, minimizing potential training, or recent acclimatization effects. Week 1 (baseline) consisted of no intervention, wherein each worker was provided with the standard 2.5 L of electrolyte solution per day (referred to locally as “suero”). During Week 2, the provided electrolyte solution amount was 5 L per day, followed by an increase to 10 L per day during Week 3. Between Weeks 1 and 2 and Weeks 2 and 3, workers had 1 day off. The electrolyte solution formula used in 2018 for all the workers consisted of 2.6 g NaCl, 2 g KCl, 13.5 g carbohydrates (glucose), and 40 kcal, per liter, based on the World Health Organization (WHO) recommended oral rehydration formula.³³ The solution was provided to the workers in powder packets that they then dissolved in filtered, chlorinated water. The workers consumed the electrolyte solution during the working shift and could supplement with plain water ad libitum throughout the day. Workers were monitored by field health aides during the workday to ensure that the electrolyte solution was consumed as directed. Ethics approval was provided by the Colorado Multiple Institutional Review Board (COMIRB) of the University of Colorado.

Data Collection

Pre- and Post-Shift Measures

Figure 1 displays the clinical measures collected for this trial. To assess changes in markers of kidney function, point-of-care (POC) creatinine was collected for each participant prior to the start of the work shift (5 to 6 am) and at the end of the work shift (4 to 5 pm) on the last day (day 6) of each of the 3 consecutive work weeks. POC creatinine was measured using the handheld Nova[®] Statscan (Stat Sensor Creatinine Meter, Nova Biomedical Corporation, Waltham, MA). Previously, we conducted a study in two similar worker cohorts to determine whether the POC creatinine meter can reliably be used to measure serum creatinine under working conditions in a rural tropical location.³⁴ Based on this previous study comparing venous and capillary samples of post-shift POC creatinine measures, we applied an adjustment factor of 0.7775 to all the post-shift capillary POC creatinine values in the current study. We derived and validated this adjustment factor in two populations of sugarcane workers in Guatemala and it resulted in better specificity

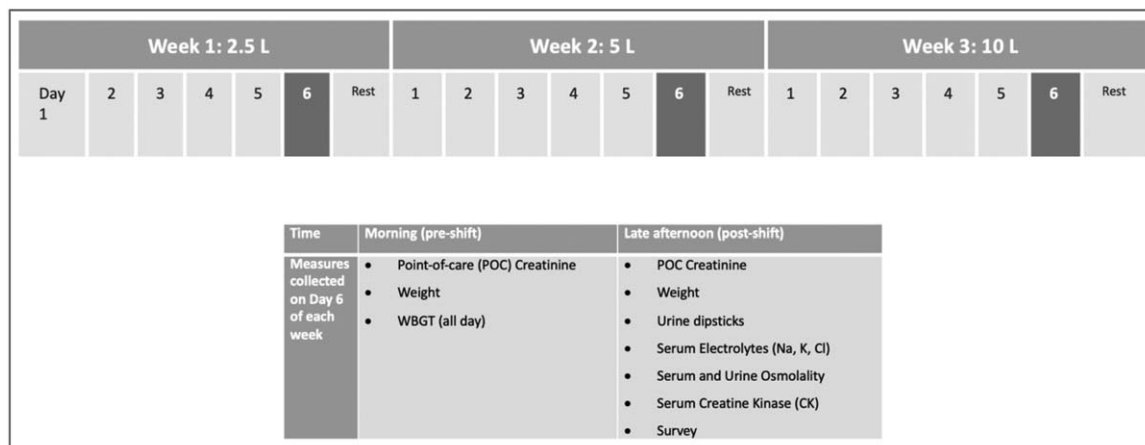


FIGURE 1. Study design.

and a better positive predictive value to relate them to venous values. In other analyses, among similar cohorts, we have observed good agreement between venous and capillary samples of creatinine measurements when they are obtained pre-work shift, thus requiring an adjustment factor of 1, or no adjustment, to relate capillary creatinine values to venous values taken at morningtime, prior to the start of work.^{35,36} To assess volume depletion across the work shift, body weight was measured using a Seca® model 874DR digital scale (Seca Corporation, Chino, California) that was placed on a stable platform and calibrated prior to the collection of data. Workers were weighed in work clothing with shin guards and shoes removed. To adjust for the extra weight of the clothes at the end of the workday due to sweat and dirt, we calculated a correction factor and subtracted the correction factor from each worker's post-shift weight result.²⁷

Post-Shift Measures and Survey

Post-shift venipuncture blood and urine samples were also collected on the last day of each week. Samples were sent on ice the same day to an independent, licensed clinical laboratory (Herrera Llerandi laboratory, Guatemala City, Guatemala). Serum blood measures included electrolytes (sodium, potassium, and chloride), creatine kinase (CK), and osmolality. Serum electrolyte concentrations were measured by ion selective electrode techniques (I-Sens, I-Smart 30 Pro), and serum CK was determined with CK-NAC serum start (DGKC) (Toche Cobas Integra 400 Plus). Serum and urine osmolality was measured using freezing point depression osmometry (Precision Systems 5004 Micro-Osmette, Norwood, MA). Urine dipsticks (Mission Urinalysis Reagent strips, ACON laboratories, San Diego, CA) measured specific gravity and pH. A survey was conducted by trained Spanish-speaking survey administrators post-shift to collect feedback and assess acceptability of the electrolyte formula as well as to collect data on fluid intake and heat-related symptoms experienced during the last day of each week.

Work Conditions and Productivity

Wet bulb globe temperature (WBGT) was measured in the field where the workers were cutting cane during the workday (3M QUESTemp 34, Thermal Environmental Monitor). The WBGT meter provided output readings on the average and maximum WBGT for each study day. The company provided investigators at the Center for Health, Work & Environment with a dataset of worker productivity that included daily tons cut for each worker for each of the 3 weeks.

Data Analysis

Data collected by Pantaleon for this trial were de-identified and then provided to the Center for Health, Work & Environment for analysis. One subject was excluded from the analysis for being

present during only one time point. The primary outcome measures were two hydration indices: low serum electrolytes (hyponatremia: serum sodium less than 135 mEq/L, hypokalemia: serum potassium less than 3.5 mEq/L, and hypochloremia: less than 97 mEq/L) and abnormal serum osmolality (hypo-osmolality less than 280 mOsm/kg; hyper-osmolality: more than 295 mOsm/kg). Secondary outcome measures were incidence of high CK (subclinical rhabdomyolysis [175 to 869 U/L] or rhabdomyolysis [more than 870 U/L], and cross-shift change in kidney function, measured by percent change in POC creatinine). As high levels of creatinine indicate worsening kidney function, a positive percent change from pre-shift to post-shift indicates a decline in kidney function.

Covariates observed were urinary specific gravity (U_{SG}), urine pH, daily average productivity per week, and worker-reported data from the survey. Post-shift U_{SG} was placed into three clinical categories (maximally dilute, less than 1.005; well hydrated, 1.005 to 1.020; and dehydrated, more than 1.020).

Descriptive statistics were calculated for all measures; the majority of the clinical data were not normally distributed and are expressed as the median and interquartile range (IQR). Paired *t* tests were used for univariate analyses to identify differences in individual clinical and biomarker data during Week 1 compared with those collected during the intervention at Weeks 2 and 3. For non-continuous data (eg, urine dipstick results), the chi-square or Fisher exact test was used to compare the weeks. Participant characteristics (ie, demographics, behavior, clinical and survey data) are described as summary statistics.

Mixed effects linear regression with random intercepts for subjects was used to assess differences between the 3 weeks while controlling for covariates. All mixed effects models controlled for average daily tons per week, age, urine specific gravity, and AM creatinine.

All analyses were performed using SAS Release 9.4 (SAS Institute, Cary, NC) or SAS Studio, University Edition 2.8 9.4 M6.

RESULTS

Baseline Characteristics and Demographics

Blood measures were collected from 48 workers during Week 1, 50 in Week 2, and 51 in Week 3. The median age of the participants was 24 years (IQR: 21 to 31). At Week 1, the median pre-shift weight was 56 kg (IQR: 53 to 60), and median body mass index (BMI) was 21.6 kg/m² (IQR: 20.0 to 23.2).

Work Conditions and Productivity

Table 1 displays work conditions and productivity during the trial period. The average amount of daily cane cut per week was lower during Week 3 compared with Weeks 1 and 2. However, based on the rate of cane cut per hour, productivity each week was approximately the same. Workers actively cut cane for 6.25 hours

TABLE 1. Work Conditions and Productivity

	Week 1 (Baseline)	Week 2	Week 3
	2.5 L Electrolyte Solution	5 L Electrolyte Solution	10 L Electrolyte Solution
	Mean (SD)		
Hours worked	6.25	7.50	6.50
Daily tons cut (week average)	7.26 (0.94)	7.19 (2.0)	5.73 (1.14)
Daily tons cut per hour worked (week average)	1.16 (0.15)	0.96 (0.27)	0.88 (0.18)
Average WBGT (°C) on study day	34.0 °C	33.2 °C	31.2 °C
Max WBGT (°C) on study day	37.9 °C	39.2 °C	38.4 °C

WBGT, wet bulb globe temperature.

TABLE 2. Hydration and Electrolyte Results and Comparison by Week

	Week 1 (Baseline)	Week 2	Week 3	W2–W1	W3–W1	W3–W2
	2.5 L	5 L	10 L	5–2.5	10–2.5	10–5
	Median (IQR) or N (%)			Comparison P-value		
Primary hydration outcomes	N = 48	N = 50	N = 51			
Osmolality (serum), mOsm/kg	274 (271, 275)	277 (271, 280)	273 (264, 279)	<0.01	0.93	<0.01
Hypo-osmolality (<280 mOsm/kg)	46 (96%)	37 (74%)	41 (80%)			
Hyper-osmolality (>295 mOsm/kg)	0%	1 (2%)	0%			
Osmolality (urine), mOsm/kg	87.50 (82.50, 157)	79 (61, 126)	82 (69, 113)	0.07	0.02	0.68
Sodium (serum), mEq/L	137.50 (135, 138)	136.50 (134, 138)	137 (135, 139)	0.06	0.91	0.07
Hyponatremia (<135 mEq/L)	9 (19%)	14 (28%)	12 (24%)			
Potassium (serum), mEq/L	4.15 (4, 4.45)	3.8 (3.5, 4)	4.20 (3.9, 4.5)	<0.01	0.61	<0.01
Hypokalemia (<135 mEq/L)	0%	11 (22%)	6 (12%)			
Chloride (serum), mEq/L	97.5 (95.50, 99)	97 (94, 99)	98 (95, 101)	0.30	0.69	0.33
Hypochloremia (<97 mEq/L)	17 (35%)	21 (42%)	20 (39%)			
Other hydration indices	N = 49	N = 50	N = 50			
Urinary specific gravity				0.88	0.63	<0.01
Maximally dilute (<1.005)	7 (14%)	7 (14%)	16 (32%)			
Normal	42 (86%)	43 (86%)	34 (68%)			
Dehydrated (>1.020)	0%	0%	0%			
pH < 7 (urine)	31 (63%)	24 (48%)	31 (62%)	0.34	0.77	0.22
% Weight change cross-shift	0.84 (–0.22, 2.31)	1.59 (0.52, 3.66)	3.13 (1.77, 4.39)	<0.01	<0.01	0.04

Bold values indicate statistical significance (*P* < 0.05).

(Week 1), 7.50 hours (Week 2), and 6.50 hours (Week 3). Average WBGT are displayed in Table 1 and ranged from 34 °C in Week 1 and 31.2 °C in Week 3 with maximum temperatures exceeding 39 °C in Week 2.

Hydration and Electrolyte Levels

Table 2 summarizes the primary hydration outcomes as well as other hydration indices observed. Figures of the primary outcomes are displayed in the supplemental digital content, <http://links.lww.com/JOM/A823>, <http://links.lww.com/JOM/A824>, <http://links.lww.com/JOM/A825>. Serum osmolality increased significantly from Week 1 to Week 2, but declined at Week 3. Hypo-osmolality (less than 280 mOsm/kg) was common: 96% in Week 1, 74% in Week 2, and 80% in Week 3. Urine osmolality declined on average with the increase in electrolyte consumption, however there were no significant differences between Weeks 2 and 3. Workers' electrolytes were within normal ranges on average during all weeks. Hyponatremia was present during all weeks (19% in Week 1, 28% in Week 2, and 24% in Week 3). Hypokalemia appeared in Week 2 (22%), and reduced to 12% in Week 3. Hypochloremia was common during all weeks (35% in Week 1, 42% in Week 2, and 39% in Week

3). Serum sodium, potassium, and chloride levels did not increase with an increase in electrolyte consumption.

Based on post-shift urinary specific gravity, no workers were dehydrated during any trial period. The percentage of workers that had maximally dilute urine increased from Week 1 to Week 3 (14% vs 32%, respectively). The percentage of workers with acidic urine (pH < 7) declined in Week 2 (63%, Week 1 to 48%, Week 2) but then increased again to 62% in Week 3. Median percent weight change across the work shift significantly increased each week (0.84% in Week 1, 1.59% in Week 2, and 3.13% in Week 3).

Kidney Function and Muscle Breakdown

Table 3 displays the results for kidney function and muscle breakdown. Pre-shift and post-shift creatinine remained stable between the weeks. Median pre-shift creatinine at Week 1 was 0.79 mg/dL, compared with 0.78 and 0.80 during Weeks 2 and 3 respectively.

Median post-shift creatinine was 0.85 mg/dL during Weeks 1 and 2, and 0.86 during Week 3. This amounted to a median increase of 5.98% in creatinine across the shift during Week 1, 8.20% in Week 2, and 7.76% in Week 3. CK levels and CK levels/hour

TABLE 3. Markers of Kidney Function and Muscle Breakdown Comparisons by Week

	Week 1 (Baseline)	Week 2	Week 3	W2–W1	W3–W1	W3–W2
	2.5 L	5 L	10 L	5–2.5	10–2.5	10–5
	Median (IQR) or N (%)			Comparison P-value		
Creatinine (morning), mg/dL	0.79 (0.77, 0.84)	0.78 (0.75, 0.81)	0.80 (0.77, 0.82)	0.71	0.92	0.37
Creatinine (afternoon), mg/dL	0.85 (0.81, 0.89)	0.85 (0.81, 0.91)	0.86 (0.82, 0.90)	0.83	0.83	0.70
% change creatinine (cross-shift)	5.98 (2.52, 11.86)	8.20 (2.95, 15.15)	7.76 (1.67, 11.39)	0.72	0.86	0.41
Creatine kinase, U/L	753 (500, 1238)	561.50 (429, 820)	311 (200, 483)	<0.01	<0.01	<0.01
Subclinical rhabdomyolysis (175–869 U/L)	27 (56%)	38 (76%)	39 (76%)			
Rhabdomyolysis (≥870 U/L)	21 (44%)	12 (24%)	4 (8%)			
Creatine kinase/h worked, U/L	120.48 (80.0, 198.08)	74.87 (57.20, 109.33)	47.85 (30.77, 74.31)	<0.01	<0.01	<0.01

IQR, interquartile range.

Bold values indicate statistical significance (*P* < 0.05).

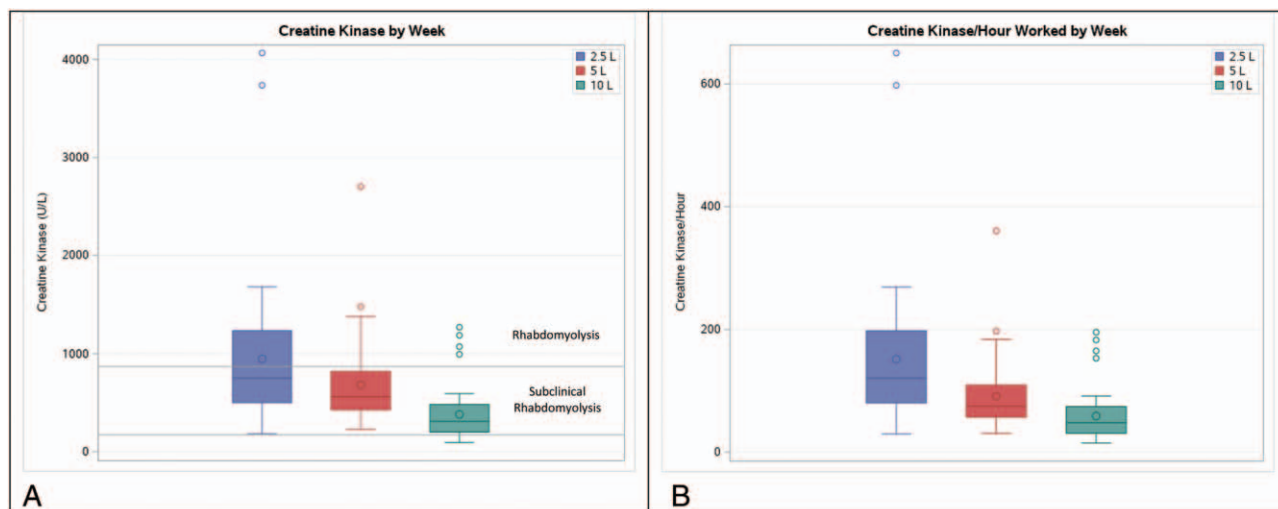


FIGURE 2. A–B: Muscle breakdown by week. A: Muscle breakdown, measured by creatine kinase (CK), by intervention week. B: Creatine kinase (CK) level (U/L) per hour worked, by intervention week.

worked declined significantly each week as the amount of electrolyte consumption increased (Fig. 2). During Week 1, the median CK level was 753 U/L (IQR: 500 to 1238 U/L) and fell to 561.50 U/L (IQR: 429 to 820 U/L) in Week 2 and to 311 U/L (IQR: 200–483 U/L) in Week 3. The frequency of rhabdomyolysis decreased from 44% in Week 1 to 24% in Week 2, reducing further to 8% in Week 3.

Mixed Effects Analyses

After adjusting for productivity, age, hydration status (U_{SG}), and pre-shift creatinine, the observed reduction in CK levels between intervention weeks continued to be significant (Table 4): from Week 2 to Week 1: (Effect: -233.26 [95% confidence interval [CI]: $-389.02, -77.50$] $P=0.003$), and Week 3 to Week 2: (Effect: -311.26 [95% CI: $-485.28, -137.24$] $P<0.001$). There were no significant differences between the weeks for average sodium or chloride levels. Serum osmolality was significantly higher in Week 2 compared with Week 1 but significantly lower in Week 3 compared with Week 2 (Effect: -4.71 [95% CI: $-7.28, -2.13$] $P<0.001$).

Survey

Forty-nine workers completed the survey in Week 1, compared with 48 in Week 2 and 34 in Week 3. As the quantity of electrolyte solution consumption increased, plain water intake changed little from Week 1 to Week 2, but decreased substantially during Week 3; 94% and 92% reported drinking more than 10 L of plain water at Weeks 1 and 2 respectively, whereas 94% reported

drinking 10 L or less by Week 3. The average total reported volume of fluid consumed (electrolytes plus plain water) differed significantly by week ($P<0.001$); volume increased from Week 1 ($17.70 \pm 2.9L$) to Week 2 (20.63 ± 3.0), and then decreased slightly during Week 3 to $18.60 \pm 2.6L$. The majority of surveyed workers (74%) reported feeling the best during Week 2 with 5 L of electrolyte solution.

Workers were also surveyed about heat-related symptoms during each day of data collection. In Week 1, 16% of workers reported weakness. In Week 2, this reduced by half to 8% of workers, and in Week 3 no workers reported weakness. However, in Week 3, 9% of workers reported nausea and 6% of headaches compared with 0% for either condition in Weeks 1 and 2. The proportion of workers reporting not having any thirst declined each week, with 86% in Week 1, 81% in Week 2, and 74% in Week 3. No workers reported feeling “very thirsty” during any week, however the number of workers reporting having some “normal thirst” increased slightly each week, from 14% and 19% during weeks 1 and 2 respectively, to 26% in Week 3. All workers (100%) reported liking the taste of the solution and did not have any problems with the preparation.

DISCUSSION

Increased consumption of electrolyte solution was associated with less muscle damage in agricultural workers carrying out intense physical effort in hot conditions. CK levels decreased each week of the study intervention with increasing consumption of

TABLE 4. Mixed Effects Linear Regression Analyses Comparing Changes in Primary Outcomes Between Intervention Weeks*

Outcome	Week 2–Week 1		Week 3–Week 1		Week 3–Week 2	
	Effect (95% CI)	P-Value	Effect (95% CI)	P-Value	Effect (95% CI)	P-Value
Sodium	-1.06 (-2.10, -0.02)	0.05	-0.05 (-1.29, 1.19)	0.94	1.01 (-0.18, 2.20)	0.09
Potassium	-0.41 (-0.59, -0.23)	<0.001	0.06 (-0.15, 0.27)	0.55	0.47 (0.27, 0.67)	<0.001
Chloride	-0.67 (-1.93, 0.59)	0.30	-0.39 (-1.88, 1.09)	0.60	0.27 (-1.15, 1.69)	0.70
Serum osmolality	2.97 (0.77, 5.16)	0.01	-1.74 (-4.44, 0.97)	0.20	-4.71 (-7.28, -2.13)	<0.001
Creatine kinase	-233.26 (-389.02, -77.50)	0.003	-544.52 (-725.58, -363.45)	<0.001	-311.26 (-485.28, -137.24)	<0.001

*Models controlled for average daily tons per week, age, urine specific gravity, and AM creatinine. Bold values indicate statistical significance ($P<0.05$).

electrolyte solution, and workers maintained serum electrolyte levels and experienced slight declines in kidney function that remained within normal limits. Workers were hydrated on average during all weeks, based on urine specific gravity, percent weight change across the shift, and serum and urine osmolality. Workers also reported less weakness. Prevention of muscle damage is especially important for this worker population that is potentially at high risk for conditions like rhabdomyolysis; additionally, maintaining euhydration is important for physical performance in the heat as hypohydration is associated with increased cardiovascular strain and declines in aerobic capacity^{37,38} and thus productivity and endurance in the occupational setting.^{7,23,39,40}

This pragmatic comparative effectiveness trial demonstrates the feasibility of maintaining workers' electrolyte levels under extremely hot and humid conditions. The intervention was achievable for the company to deliver and acceptable to workers, while overall productivity was also preserved. Most of the existing research on the topic of electrolyte supplementation has been among elite athletes, and yet agricultural worker populations are especially vulnerable for the same reasons as elite athletes, in addition to the fact that they may have less access to quality hydration sources and are at higher risk for food insecurity, unstable income, and inadequate nutrition.^{41–43} Recommendations to mitigate the risks faced by agricultural workers laboring in the heat from OSHA and NIOSH include guidance around water/rest/shade, heat exposure assessment, and heat-related illness education and monitoring; however, the guidance around hydration and especially electrolyte replacement is unclear. There is not currently a national standard or enforcement in the United States around occupational heat exposure for any industry, other than when OSHA invokes the General Duty Clause.²⁴ Some of the best-known heat-related mitigation strategies originate from the field of exercise physiology, including recommendations around electrolyte intake.^{44–48} The importance of occupational heat acclimatization has been studied among firefighters, although these studies have not specifically addressed electrolyte intake.^{49,50} Less is known of what is needed to protect those carrying out other forms of work in the heat, daily, for prolonged periods of time.

Despite prolonged exposure to hot, humid temperatures, and physical exertion, this group of 50 workers did not experience any significant renal impairment. In fact, the increase in electrolytes appeared to have little effect on renal function either way. We do not know if the provision of electrolytes helped prevent kidney injury, however we recognize that this was a small cohort and was not powered to answer that question. Based on our previous research in this population,^{27,28} we were surprised not to see significant cross-shift kidney injury during the baseline week. We acknowledge that participants may have modified their behavior in ways that we did not measure as a result of the extra attention they received from observers during the evaluation days (ie, observer or "Hawthorne" effect) although these workers are generally accustomed to being observed by clinical staff as part of the company's existing health surveillance programs.

Hypo-osmolality and weight gain across the work shift were common during all weeks of this evaluation, indicating that workers would be considered to be overhydrating both before and after the intervention was implemented. Of particular note, asymptomatic hyponatremia was common throughout the trial. Hyponatremia itself is associated with a number of adverse health effects including exertional rhabdomyolysis, although the evidence is mixed as to whether one causes the other or whether they occur independently.^{13–16,51–55} In this study, electrolyte levels did not increase on average with the increase in electrolyte solution, most likely because workers were in the habit of drinking large quantities of plain water, despite being encouraged to only consume plain water when they had persistent thirst. As a result, it is possible, although

unlikely, that the reduction in CK could be attributed to dilution in the blood and/or plasma volume expansion (water retention). Calculating the expected CK in the presence of plasma volume expansion (5 to 5.5 L)⁴⁴ results in lower values for Weeks 2 and 3 than what we observed (620.96 and 346.81 U/L respectively), indicating that plasma volume expansion does not fully explain the reduction in CK seen in this trial. Furthermore, we observed a decrease in workers with hypo-osmolality from Week 1 (96%) to 74% in Week 2 and 80% in Week 3, as well as a decrease in morning body mass, and we did not observe a similar reduction in electrolytes and creatinine, adding further evidence against a dilution effect. The question therefore remains whether hyperhydration (excess fluid intake) could play some protective role in this setting among this worker population. A few published studies support the hypothesis that fluid overload may be beneficial particularly in hot environments by increasing body water reserves and assisting the body with temperature regulation.^{56–59} In our evaluation, the additional fluid and added electrolytes appear to reduce skeletal muscle damage. As a result of this trial, moving forward, the employer is educating workers to reduce plain water consumption in favor of increased electrolyte solution use. As workers become better accustomed to consuming less plain water and instead replacing it with electrolyte solutions, we expect to see improvement in serum electrolyte levels. Another important next step in this research is to evaluate the nutrition status of these workers in order to examine intake of electrolytes through their diet. It may be that additional nutrition could have similar beneficial effects.⁶⁰

Heat-related illness and injury, dehydration, and high incidence of exertional muscle breakdown are some of the adverse health impacts known to be experienced by outdoor sugarcane workers.^{28,29,61–67} These health impacts have been implicated as potential risk factors for acute kidney damage that may result in chronic kidney disease of unknown cause (CKDu), also known as Mesoamerican nephropathy, that is affecting agricultural workers and especially sugarcane workers globally.^{3,9,28,68–71} Findings from our prior research found that while the provision of water, rest, and shade in the field was partially protective, a high incidence (81%) of acute kidney injury (AKI) was observed across the work shift.^{27,28} Importantly, higher electrolyte solution intake was also found to be at least partially protective against AKI among these workers, similar to findings in a study conducted among sugarcane workers in Brazil.²⁹ In the Brazilian study, low serum sodium was more common among workers with AKI, compared with those without AKI. The authors noted that low serum sodium could potentially worsen intravascular volume depletion that results from decreased plasma osmolality. Lower plasma osmolality has been shown to be associated with higher serum CK levels among endurance athletes.⁷² Other studies among sugarcane cutters have found electrolyte fluid intake to be associated with improved kidney function biomarkers.^{66,73,74} A recent study in Nicaragua found that a hydration, rest, and shade intervention that included increased electrolyte solution intake was associated with reduced risk for incident kidney injury across the season.³⁰ That study did not collect information on non-renal health outcomes such as CK, serum electrolytes, or serum osmolality. More research is needed on the potential protective effects of electrolyte solutions on the prevention of kidney injury as well as other health outcomes in this worker population.

One objective of our work is to improve recommendations for prevention of heat-related illness and other climate adaptation techniques that can be applied to agricultural workers. The purpose of this evaluation was to determine the appropriate water and electrolyte regimen for this worker population in order to mitigate muscle injury without deleterious effects on measures of electrolytes, kidney function, or productivity. The results show that an increase in electrolyte solution may be effective in reducing muscle breakdown and self-reported weakness, although higher levels of

intake may slightly increase risk for headaches and nausea. Between 5 and 10 L is recommended for this population of sugarcane workers in this environment under this level of physical exertion, however there are also many foods to consider that can supply needed electrolytes. This evaluation was designed as a trial to assess the efficacy of the enhanced hydration program; the next step is to test the effectiveness of the intervention with a larger population and evaluate the implementation and impact of the program across the company. An additional next step for this line of research is an assessment of electrolyte loss through sweat during a work shift. The rate and quantity of electrolytes lost in sweat can be highly variable between individuals, and can be further influenced by acclimatization.^{21,25}

This study carries several additional limitations. We evaluated a small cohort of workers who were from the same home community; therefore, the results of this study may not be generalizable to other farmworker populations. In particular, this study was conducted among a group of workers who originate from a community in the highland regions of Guatemala. We know from our previous research that workers from highland communities of Guatemala tend to have better renal health outcomes than workers living in coastal communities near the sugarcane plantations. However, due to the fact that we were able to see benefit in this otherwise healthy working population, it stands to reason that we may see an even more dramatic protective benefit in a less healthy, more at-risk population. As in many studies of heat-related illness in farmworker populations, heat exposure was assessed through the WBGT and self-reported heat-related symptoms. Few workers reported experiencing any symptoms; it is possible that workers feel uncomfortable reporting such symptoms to their employer. More robust exposure assessment methods to precisely quantify heat exposure magnitude in farmworkers, such as through the ingestible temperature monitoring pill, are greatly needed.^{9,75} This information can help us determine the level of heat strain, or the body's physiological response to heat stress, in workers by continuously monitoring core body temperature and heart rate.

CONCLUSION

There is increasing recognition that with globally rising temperatures, electrolyte replacement will be important for workers that are exposed to heat. To our knowledge, this is one of the few studies outside of a laboratory or highly controlled setting to examine the effect of electrolyte replacement in workers under extreme conditions of heat, humidity, and physical labor. Larger studies of this kind are needed in agricultural workers. It is critical to understand the role that volume and electrolyte losses during the workday contribute to the onset of heat-related illness in order to improve upon existing acclimatization and occupational hydration/rest/shade programs and policies designed to prevent injury. Based on the results of this study, we recommend that a new standard for outdoor workers be developed and evaluated that includes electrolyte provision in addition to the current water, rest, and shade guidelines, including programs to educate workers of their importance. Although this was a small study, the results have important implications for climate adaptation and risk mitigation for outdoor laborers who are especially vulnerable to the effects of rising temperatures and other impacts of climate change.

REFERENCES

- Kiefer M, Rodríguez-Guzmán J, Watson J, van Wendel de Joode B, Mergler D, da Silva AS. Worker health and safety and climate change in the Americas: issues and research needs. *Rev Panam Salud Publica*. 2016;40:192–197.
- International Labour Organization (ILO). *Climate Change and Labour: Impacts of Heat in the Workplace*. United Nations Development Programme; 2016.
- Butler-Dawson J, Krisher L, Asensio C, et al. Risk factors for declines in kidney function in sugarcane workers in Guatemala. *J Occup Environ Med*. 2018;60:548–558.
- Correa-Rotter R, Wesseling C, Johnson RJ. CKD of unknown origin in Central America: the case for a Mesoamerican nephropathy. *Am J Kidney Dis*. 2014;63:506–520.
- Crowe J, Wesseling C, Solano BR, et al. Heat exposure in sugarcane harvesters in Costa Rica. *Am J Ind Med*. 2013;56:1157–1164.
- Hansson E, Glaser J, Weiss I, et al. Workload and cross-harvest kidney injury in a Nicaraguan sugarcane worker cohort. *Occup Environ Med*. 2019;76:818–826.
- Dally M, Butler-Dawson J, Krisher L, et al. The impact of heat and impaired kidney function on productivity of Guatemalan sugarcane workers. *PLoS One*. 2018;13:e0205181.
- Kjellstrom T, Crowe J. Climate change, workplace heat exposure, and occupational health and productivity in Central America. *Int J Occup Environ Health*. 2011;17:270–281.
- Moyce S, Mitchell D, Armitage T, Tancredi D, Joseph J, Schenker M. Heat strain, volume depletion and kidney function in California agricultural workers. *Occup Environ Med*. 2017;74:402–409.
- Ganio MS, Armstrong LE, Casa DJ, et al. Mild dehydration impairs cognitive performance and mood of men. *Br J Nutr*. 2011;106:1535–1543.
- Schulte PA, Bhattacharya A, Butler CR, et al. Advancing the framework for considering the effects of climate change on worker safety and health. *J Occup Environ Hyg*. 2016;13:847–865.
- Claremont AD, Costill DL, Fink W, Van Handel P. Heat tolerance following diuretic induced dehydration. *Med Sci Sports*. 1976;8:239–243.
- Chlíbková D, Knechtel B, Rosemann T, et al. Rhabdomyolysis and exercise-associated hyponatremia in ultra-bikers and ultra-runners. *J Int Soc Sports Nutr*. 2015;12:29.
- Ellis C, Cuthill J, Hew-Butler T, George SM, Rosner MH. Case report: exercise-associated hyponatremia with rhabdomyolysis during endurance exercise. *Phys Sportsmed*. 2009;37:126–132.
- Hoffman MD, Stuempfle KJ. Sodium supplementation and exercise-associated hyponatremia during prolonged exercise. *Med Sci Sports Exerc*. 2015;47:1781–1787.
- Hoffman MD, Stuempfle KJ, Sullivan K, Weiss RH. Exercise-associated hyponatremia with exertional rhabdomyolysis: importance of proper treatment. *Clin Nephrol*. 2015;83:235–242.
- Bosch X, Poch E, Grau JM. Rhabdomyolysis and acute kidney injury. *N Engl J Med*. 2009;361:62–72.
- Patel DR, Gyamfi R, Torres A. Exertional rhabdomyolysis and acute kidney injury. *Phys Sportsmed*. 2009;37:71–79.
- Clarkson PM. Exertional rhabdomyolysis and acute renal failure in marathon runners. *Sports Med*. 2007;37:361–363.
- de Meijer AR, Fikkers BG, de Keijzer MH, van Engelen BGM, Drenth JPH. Serum creatine kinase as predictor of clinical course in rhabdomyolysis: a 5-year intensive care survey. *Intensive Care Med*. 2003;29:1121–1125.
- Maughan RJ, Shirreffs SM. Recovery from prolonged exercise: restoration of water and electrolyte balance. *J Sports Sci*. 1997;15:297–303.
- Occupational Safety and Health Administration. OSHA Technical Manual (OTM) | Section III: Chapter 4 - Heat Stress | Occupational Safety and Health Administration. Occupational Safety and Health Administration; 2017. Available at: https://www.osha.gov/dts/osta/otm/otm_iii/otm_iii_4.html. Accessed November 11, 2018.
- National Institute for Occupational Safety and Health (NIOSH). *Criteria for a Recommended Standard: Occupational Exposure to Heat and Hot Environments - Revised Criteria 2016*. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health; 2016.
- Occupational Safety and Health Administration. OSHA's Campaign to Prevent Heat Illness in Outdoor Workers | Protective Measures to Take at Each Risk Level. Available at: https://www.osha.gov/SLTC/heatillness/heat_index/protective_measures.html. Accessed June 12, 2020.
- American College of Sports Medicine, Sawka MN, Burke LM, et al. American College of Sports Medicine position stand. Exercise and fluid replacement. *Med Sci Sports Exerc*. 2007;39:377–390.
- Casa DJ, Armstrong LE, Hillman SK, et al. National athletic trainers' association position statement: fluid replacement for athletes. *J Athl Train*. 2000;35:212–224.
- Butler-Dawson J, Krisher L, Yoder H, et al. Evaluation of heat stress and cumulative incidence of acute kidney injury in sugarcane workers in Guatemala. *Int Arch Occup Environ Health*. 2019;92:977–990.

28. Sorensen CJ, Butler-Dawson J, Dally M, et al. Risk factors and mechanisms underlying cross-shift decline in kidney function in Guatemalan sugarcane workers. *J Occup Environ Med*. 2019;61:239–250.
29. Paula Santos U, Zanetta DMT, Terra-Filho M, Burdmann EA. Burnt sugarcane harvesting is associated with acute renal dysfunction. *Kidney Int*. 2015;87:792–799.
30. Glaser J, Hansson E, Weiss I, et al. Preventing kidney injury among sugarcane workers: promising evidence from enhanced workplace interventions. *Occup Environ Med*. 2020;77:527–534.
31. Patsopoulos NA. A pragmatic view on pragmatic trials. *Dialogues Clin Neurosci*. 2011;13:217–224.
32. Chang TI, Winkelmayr WC. Comparative effectiveness research: what is it and why do we need it in nephrology? *Nephrol Dial Transplant*. 2012;27:2156–2161.
33. World Health Organization. *WHO Drug Information*. Vol 16; 2002, 91. <https://www.who.int/medicines/publications/druginformation/en/>. Accessed December 30, 2019.
34. Griffin BR, Butler-Dawson J, Dally M, et al. Unadjusted point of care creatinine results overestimate acute kidney injury incidence during field testing in Guatemala. *PLoS One*. 2018;13:e0204614.
35. Butler-Dawson J. Additional information about POC creatinine measures prior to the start of the work shift. *PLoS One*. 2019. <https://journals.plos.org/plosone/article/comment?id=10.1371/annotation/35061b06-beec-49a8-881a-d13d5f28546d>. Accessed March 10, 2020.
36. Dally M, Butler-Dawson J, Johnson RJ, et al. Creatinine fluctuations forecast cross-harvest kidney function decline among sugarcane workers in Guatemala. *Kidney Int Rep*. 2020;5:1558–1556.
37. Sawka MN, Coyle EF. Influence of body water and blood volume on thermoregulation and exercise performance in the heat. *Exerc Sport Sci Rev*. 1999;27:167–218.
38. Chevront SN, Carter R, Sawka MN. Fluid balance and endurance exercise performance. *Curr Sports Med Rep*. 2003;2:202–208.
39. Quiller G, Krenz J, Ebi K, et al. Heat exposure and productivity in orchards: Implications for climate change research. *Arch Environ Occup Health*. 2017;72:313–316.
40. Kjellstrom T, Kovats RS, Lloyd SJ, Holt T, Tol RS. The direct impact of climate change on regional labor productivity. *Arch Environ Occup Health*. 2009;64:217–227.
41. Arcury TA, Summers P, Talton JW, et al. Heat illness among north carolina latino farmworkers. *J Occup Environ Med*. 2015;57:1299–1304.
42. Villarejo D. The health of U.S. hired farm workers. *Annu Rev Public Health*. 2003;24:175–193.
43. Villarejo D, McCurdy SA, Bade B, Samuels S, Lighthall D, Williams D. The health of California's immigrant hired farmworkers. *Am J Ind Med*. 2010;53:387–397.
44. Tyler CJ, Reeve T, Hodges GJ, Cheung SS. The effects of heat adaptation on physiology, perception and exercise performance in the heat: a meta-analysis. *Sports Med*. 2016;46:1699–1724.
45. Lorenzo S, Halliwill JR, Sawka MN, Minson CT. Heat acclimation improves exercise performance. *J Appl Physiol*. 2010;109:1140–1147.
46. Burk A, Timpmann S, Kreegipuu K, Tamm M, Unt E, Öpik V. Effects of heat acclimation on endurance capacity and prolactin response to exercise in the heat. *Eur J Appl Physiol*. 2012;112:4091–4101.
47. Sawka MN, Latzka WA, Montain SJ, et al. Physiologic tolerance to uncompensable heat: intermittent exercise, field vs laboratory. *Med Sci Sports Exerc*. 2001;33:422–430.
48. Cheung SS, McLellan TM. Heat acclimation, aerobic fitness, and hydration effects on tolerance during uncompensable heat stress. *J Appl Physiol*. 1998;84:1731–1739.
49. Lui B, Cuddy JS, Hailes WS, Ruby BC. Seasonal heat acclimatization in wildland firefighters. *J Therm Biol*. 2014;45:134–140.
50. Brearley MB, Norton I, Rush D, et al. Influence of chronic heat acclimatization on occupational thermal strain in tropical field conditions. *J Occup Environ Med*. 2016;58:1250–1256.
51. Bruso JR, Hoffman MD, Rogers IR, Lee L, Towle G, Hew-Butler T. Rhabdomyolysis and hyponatremia: a cluster of five cases at the 161-km 2009 Western States endurance run. *Wilderness Environ Med*. 2010;21:303–308.
52. Boulter J, Noakes TD, Hew-Butler T. Acute renal failure in four Comrades Marathon runners ingesting the same electrolyte supplement: coincidence or causation? *S Afr Med J*. 2011;101:876–878.
53. Putterman C, Levy L, Rubinger D. Transient exercise-induced water intoxication and rhabdomyolysis. *Am J Kidney Dis*. 1993;21:206–209.
54. Siegel AJ. Exercise-associated hyponatremia: role of cytokines. *Am J Med*. 2006;119(7 suppl 1):S74–S78.
55. Siegel AJ, Verbalis JG, Clement S, et al. Hyponatremia in marathon runners due to inappropriate arginine vasopressin secretion. *Am J Med*. 2007;120:461.e11–461.e17.
56. Rico-Sanz J, Frontera WR, Rivera MA, Rivera-Brown A, Mole PA, Meredith CN. Effects of hyperhydration on total body water, temperature regulation and performance of elite young soccer players in a warm climate. *Int J Sports Med*. 1996;17:85–91.
57. Latzka WA, Sawka MN, Montain SJ, et al. Hyperhydration: tolerance and cardiovascular effects during uncompensable exercise-heat stress. *J Appl Physiol*. 1998;84:1858–1864.
58. Kristal-Boneh E, Glusman JG, Shitrit R, Chaemovitz C, Cassuto Y. Physical performance and heat tolerance after chronic water loading and heat acclimation. *Aviat Space Environ Med*. 1995;66:733–738.
59. Burke LM. Nutritional needs for exercise in the heat. *Comp Biochem Physiol A Mol Integr Physiol*. 2001;128:735–748.
60. Pasiakos SM, Margolis LM, Orr JS. Optimized dietary strategies to protect skeletal muscle mass during periods of unavoidable energy deficit. *FASEB J*. 2015;29:1136–1142.
61. García-Trabanino R, Jarquín E, Wesseling C, et al. Heat stress, dehydration, and kidney function in sugarcane cutters in El Salvador—a cross-shift study of workers at risk of Mesoamerican nephropathy. *Environ Res*. 2015;142:746–755.
62. Wesseling C, Aragón A, González M, et al. Kidney function in sugarcane cutters in Nicaragua—a longitudinal study of workers at risk of Mesoamerican nephropathy. *Environ Res*. 2016;147:125–132.
63. Wegman DH, Apelqvist J, Bottai M, et al. Intervention to diminish dehydration and kidney damage among sugarcane workers. *Scand J Work Environ Health*. 2018;44:16–24.
64. Glaser J, Lemery J, Rajagopalan B, et al. Climate change and the emergent epidemic of CKD from heat stress in rural communities: the case for heat stress nephropathy. *Clin J Am Soc Nephrol*. 2016;11:1472–1483.
65. Crowe J, Nilsson M, Kjellstrom T, Wesseling C. Heat-related symptoms in sugarcane harvesters. *Am J Ind Med*. 2015;58:541–548.
66. Wesseling C, Aragón A, González M, et al. Heat stress, hydration and uric acid: a cross-sectional study in workers of three occupations in a hotspot of Mesoamerican nephropathy in Nicaragua. *BMJ Open*. 2016;6:e011034.
67. Roncal-Jimenez C, García-Trabanino R, Barregard L, et al. Heat stress nephropathy from exercise-induced uric acid crystalluria: a perspective on Mesoamerican nephropathy. *Am J Kidney Dis*. 2016;67:20–30.
68. Johnson RJ, Wesseling C, Newman LS. Chronic kidney disease of unknown cause in agricultural communities. *N Engl J Med*. 2019;380:1843–1852.
69. Mix J, Elon L, Vi Thien Mac V, et al. Hydration status, kidney function, and kidney injury in florida agricultural workers. *J Occup Environ Med*. 2018;60:e253–e260.
70. Roncal-Jimenez C, Lanaspá MA, Jensen T, Sanchez-Lozada LG, Johnson RJ. Mechanisms by which dehydration may lead to chronic kidney disease. *Ann Nutr Metab*. 2015;66(suppl):10–13.
71. Johnson RJ, Sánchez-Lozada LG, Newman LS, et al. Climate change and the kidney. *Ann Nutr Metab*. 2019;74(suppl):38–44.
72. Hoffman MD, Ingwerson JL, Rogers IR, Hew-Butler T, Stuempfle KJ. Increasing creatine kinase concentrations at the 161-km Western States Endurance Run. *Wilderness Environ Med*. 2012;23:56–60.
73. Laws RL, Brooks DR, Amador JJ, et al. Biomarkers of kidney injury among nicaraguan sugarcane workers. *Am J Kidney Dis*. 2016;67:209–217.
74. Laws RL, Brooks DR, Amador JJ, et al. Changes in kidney function among Nicaraguan sugarcane workers. *Int J Occup Environ Health*. 2015;21:241–250.
75. Mac VVT, Tovar-Aguilar JA, Flocks J, Economos E, Hertzberg VS, McCauley LA. Heat exposure in central florida fernery workers: results of a feasibility study. *J Agromed*. 2017;22:89–99.