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Wearable sensing during urban 20-km runs shows physiological strain and inhaled PM2.5 are associated with sex-specific kidney function changes

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Wearable sensing during urban 20-km runs shows physiological strain and inhaled PM2.5 are associated with sex-specific kidney function changes

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Abstract

Repeated exposure to elevated heat and $PM_{2.5}$ air pollution can harm health, and long-distance runners training outdoors face fluctuating heat stress and air quality that may threaten kidney function. Fourteen participants (seven men, seven women) each ran a pre-defined 20-km route through New York City three times at one-week intervals. Wearable sensors continuously captured ambient, wet-bulb, and core temperature, running speed, minute ventilation, heart rate, and $PM_{2.5}$, and blood and urine were collected before and after each run. Mixed-effects Weighted Quantile Sum (WQS) regression evaluated multi-exposure mixture effects on serum creatinine and tubular damage biomarkers (IL-18, KIM-1, MCP-1, YKL-40). Median wet-bulb temperature was 20.9°C (9.5–25.0°C) and median inhaled $PM_{2.5}$ mass was 102.6 µg (12.1–591.3 µg). All baseline serum creatinine values were within normal ranges, yet 14 of 42 runs (33%) met AKIN Stage 1 acute kidney injury criteria. Segment-specific WQS models suggested sex-specific responses: declines in kidney function were associated mainly with physiological strain (heart rate, speed) in men and with inhaled $PM_{2.5}$ mass in women. Tubular damage biomarkers were not significantly associated with environmental or effort-based exposures at this distance. Individualized exposure assessment may help guide exercise during adverse environmental conditions such as wildfire smoke and heatwaves.

Introduction

Exercise is one of the most beneficial activities for overall health, reducing the risk of heart disease, depression, dementia, diabetes, cancer, and other cardio-respiratory diseases. Determining how exercise under adverse environmental conditions (i.e., high air pollution or extreme heat) may diminish the benefits of training or potentially cause acute harm is challenging. Climate change models predict that the frequency and intensity of extreme heat events is increasing and will continue to increase in higher latitudes, affecting large metropolitan areas in the temperate zone where infrastructure and human biology and behavior are not adapted to hotter temperatures [1]. Additionally, recent trends in ambient air quality and particulate matter with diameters less than 2.5 μm ($PM_{2.5}$) have remained stable or increased throughout much of the United States [2-5]. Acute air pollution exposures can result in cardiovascular, respiratory, or kidney disease in general populations, leading to hospitalization or mortality [5-7]. Prolonged and acute exposure to high ambient temperatures has also been associated with adverse health outcomes, including dehydration, hypotension, renal failure, and in severe cases, heat stroke or death [8].

Exposure to elevated ambient temperature strains thermoregulatory and cardiovascular systems due to a reduced capacity for heat dissipation via evaporative cooling. Increased blood flow to the skin promotes sweating; however, high humidity can limit evaporation, causing accelerated dehydration coupled with heat retention [9]. Preferential blood flow toward the skin may also alter perfusion to other organs, leading to cell damage, tissue death (necrosis), and dysfunction or even failure of primarily the kidney, heart and brain. Additionally, exposure to $PM_{2.5}$ is associated with systemic inflammation and oxidative stress, facilitated by its ability to penetrate deep into the lungs and enter the bloodstream [10], from which it can deposit into kidney tissue [11]. Both short- and long-term exposure to $PM_{2.5}$ have been correlated with arterial vasoconstriction and elevated blood pressure, reflecting compensatory responses to maintain perfusion to vital organs [12].

Physical exertion can exacerbate physiological responses to environmental exposures via increased respiratory rate, metabolic heat production, and circulatory demand. As ventilation increases during exercise, the inhaled dosage of $PM_{2.5}$ rises with a constant ambient concentration [13]. Simultaneously, exercise-generated heat adds to environmental heat load, increasing reliance on evaporative cooling. At the onset of exercise, metabolic heat production immediately outpaces dissipation, causing rapid heat storage and an initial spike in core temperature. As the body activates heat-dissipating reflexes, heat storage slows until dissipation balances production, establishing a stable core temperature plateau if environmental conditions permit [14]. These combined demands may amplify the physiological impact of environmental stressors compared to resting conditions [15].

The kidneys may be particularly vulnerable to combined environmental and physiological stress due to their high metabolic demand and reliance on tightly regulated blood flow. Heat stress

related vasoconstriction can reduce renal perfusion, while $PM_{2.5}$ has been associated with tubular injury and inflammation implicated in acute kidney injury (AKI) [16]. Renal biomarkers may therefore be helpful in characterizing subclinical physiological responses [17] and early pathways relevant to AKI.

Despite growing evidence on the independent effects of heat exposure, air pollution, and physical exertion on human health, the joint effects of these stressors on kidney function in runners under real-world exercise conditions remain poorly understood. For example, a systematic review of outdoor exercise in environments with high traffic-related air pollution reported increased markers of respiratory and systemic inflammation and vascular dysfunction among healthy adults exercising in polluted conditions but did not assess renal outcomes or the combined effects of particulate and thermal stressors [18]. Similarly, Remigio *et al.* examined the joint effects of air pollution and extreme heat events on mortality among patients with end-stage kidney disease, demonstrating heightened risk during periods of concurrent exposure, but did not assess potential additive effects of physiological stress responses [19]. Athletes who exercise regularly outdoors may be particularly vulnerable to the health effects of increased heat exposure, as strenuous physical exertion in hot environments can result in heat stroke or AKI [20-22]. Previous studies have found that a high proportion of runners evaluated post-marathon had positive urine microscopy for acute tubular injury and AKI [22-24]. Moreover, in a recent study, runners with AKI had a longer history of running, a greater participation in marathons, and more extensive training, compared to runners without AKI (median running experience 10 vs. 6 years) [22]. However, little is known about how specific environmental conditions during training runs influence acute kidney responses.

This study examined the association between repeated exposures to urban ambient heat and $PM_{2.5}$ during three 20-km training runs with biomarkers for kidney function in New York City, New York, USA (NYC). Additionally, we applied a novel extension of Weighted Quantile Sum (WQS) regression to evaluate the association between participant-specific physiological and environmental exposure mixtures, as measured by wearable devices, with kidney function.

Methods

Study Participants

Runners of all abilities training for a half or full marathon were recruited from running clubs throughout NYC, via word of mouth and online. Participants met inclusion criteria if they ran at least 30 miles per week and were above 18 years old prior to baseline. Runners were excluded if they used nonsteroidal anti-inflammatory drugs 24 hours prior to baseline or run event, or if they had a pre-existing health condition, such as high blood pressure, heart disease, seizures, kidney disease, or stomach disorders. We aimed to recruit 18 runners, 9 male and 9 female, with four biological samples collected per runner (baseline and 3 runs). Participants attended a baseline

visit to collect initial samples and anthropometric measurements and returned approximately 1 week apart to complete three total 20-km runs each. Runners were not to undergo a training run within 24 hours of their scheduled run start time. Run events were performed from May 1 to September 30, 2023. Run events were rescheduled if the Air Quality Index (AQI) at run start was greater than 150, corresponding to the EPA threshold for unhealthy air pollution exposure [25]. Participants were compensated upon completion of each study visit: $50 after the baseline visit, $75 after Run 1, $100 after Run 2, and $125 after Run 3. All methods were performed in accordance with the relevant guidelines and regulations and with the Declaration of Helsinki. Informed consent was obtained from all study participants during their baseline visit. Protocols for cohort recruitment were approved by the institutional review board of the Icahn School of Medicine at Mount Sinai (STUDY-21-01725).

Run Route

All participants followed the pre-defined 20-km outdoor route beginning and ending in northeast Central Park, NYC (Figure S1). The route incorporated both park and urban segments, passing through Central Park, West Harlem, the West Side Highway, Hudson River Waterfront Greenway, and the Upper West Side of Manhattan.

The route was divided into regions corresponding to transitions in built and natural environments, used for spatial aggregation of environmental and physiological measures:

- Park/Green Space (14.5-km total): Comprises the initial 10-km Central Park loop (Reservoir/Bridle Path), Morningside Park (1.5-km), Riverside Park (1-km), and the final return through Central Park (2-km).
- Bike Path (3.0-km total): A continuous, traffic-separated southbound segment along the Hudson River Waterfront Greenway.
- Urban Streets (2.5-km total): Encompasses the remaining city street connections, including the Central Park-to-Morningside link, a stretch along Amsterdam Avenue and 125th Street, and a 1.5-km traverse eastward through the Upper West Side.

Clinical and Anthropometric Measurements

Clinical and anthropometric measurements were obtained at the baseline visit and before and after each run to characterize participant physiology and hydration status. Height, weight, and body composition were measured at the baseline visit, while body weight and composition were measured immediately before and after each run using an InBody Dial H20 Smart Body Composition Scale. To ensure measurement consistency and eliminate the weight of retained sweat, participants changed into the same set of dry clothing for both pre- and post-run weigh-ins. Sweat rate and water loss were calculated by adjusting the change in pre- and post-run body mass for total water intake and urination volume (all in kilograms) during the run event, Equation 1.

$$water_{lost} = bodyW_{pre} - bodyW_{post} + water_{pre} - water_{post} - urine \quad \textbf{(Eq. 1)}$$

Serum comprehensive metabolic panels and urine spot creatinine were measured after each run and compared to baseline. Serum and urine creatinine levels were used to assess hydration and identify potential changes in renal function and related physiological responses. Specifically, acute changes in kidney function were assessed using the Acute Kidney Injury Network (AKIN) threshold for Stage 1 AKI, defined as an absolute increase in serum creatinine of 0.3 $mg * dL^{-1}$ from baseline. Because clinical definitions of renal stress span both functional drops in filtration and direct cellular strain, urine samples were concurrently analyzed for tubular injury kidney biomarkers, including interleukin-18 (IL-18), kidney injury molecule-1 (KIM-1), monocyte chemoattractant protein-1 (MCP-1), and chitinase-3-like protein 1 (YKL-40). All biomarkers were measured using the Meso Scale Discovery platform (MSD, Gaithersburg, MD). To account for variability in hydration levels across sampling time points, biomarker concentrations were normalized to urine creatinine prior to analysis.

Wearable Sensors and Environmental Monitoring

Prior to each run, participants were equipped with wearable sensors to continuously measure physiological, performance, and environmental exposures (Table S1). Sensors were activated at least five minutes before the start of each run and remained active throughout the run and five minutes afterward to capture resting and recovery conditions.

Physiological measurements, including heart rate, core body temperature, and minute ventilation, were used to assess strain on cardiovascular, thermoregulatory, and respiratory processes during exercise. Running performance and movement were characterized using speed, power, GPS position, and distance traveled. Distance was used primarily to support data quality assessment and confirmation of adherence to the predefined route. Environmental exposures included ambient temperature, wet-bulb temperature, and $PM_{2.5}$ concentration.

Given the potential for signal interference or equipment failure in a complex urban environment, we utilized redundant sensors for primary exposure metrics to ensure data continuity. A pre-defined hierarchy based on signal stability during high-intensity movement, sampling frequency, and data completeness was applied to select primary sensors or substitute secondary devices when signal loss occurred (Tables S2 and S3). Detailed sensor specifications, manufacturer details, and device-specific calibration protocols are provided in the Supplementary Material.

Data Quality Assessment

Raw sensor time-series data were synchronized by aligning device timestamps to a GPS watch, used to define the start and end timepoints of the run. Standardized cleaning protocols were applied to trim initial sensor calibration windows (first 15-30 seconds) and filter physiologically improbable measurements. High-frequency optical sensor-derived $PM_{2.5}$ concentration measurements were adjusted using filter sample masses generated via gravimetric analysis, with

multiple runs loaded onto individual filters to provide sufficient mass for detection (Equations S1 and S2).

Exposure profiles were generated for each individual run event using measured values from environmental sensors. Agreement between primary and secondary sensors was evaluated using Bland-Altman analysis of concurrent measurements (Table S3). Limits of Agreement (LoA) were defined as ± 1.96 standard deviations of the mean bias.

Secondary sensors were considered interchangeable when the LoA fell within the combined manufacturer-reported accuracy ranges of the compared sensors. When these criteria were met, secondary sensor data were used to supplement or replace primary measurements in the event of signal loss or equipment failure. This approach ensured continuity of exposure definitions while maintaining consistent measurement criteria across run events.

Exposure Profiles

Exposure profiles were summarized across the entire 20-km run to generate whole-run exposure metrics.

Data were aggregated across the three built environment categories (Figure S1) to explore spatial variability. For temporal analyses, exposures were further aggregated by Early and Late 10-km phases. The first half (Early run) consisted of the initial 10-km in Central Park, while the second half (Late run) comprised the remaining 10-km and included predominantly city streets in West Harlem and the Upper West Side.

Finally, GPS position data were aggregated to 0.001° grids to allow for fine-scale comparison across run events. To maintain spatial alignment in high-density urban areas (e.g., the Upper West Side), data were aggregated into street-level bins rather than individual grid cells to account for minor variations in participant routing. Grid-level summaries were used to support the visualization and descriptive assessment of exposure patterns associated with differences in land use.

Personal vs. Longitudinal Exposures

We compared high-resolution sensor data collected during participant exercise with long-term average environmental conditions derived from static satellite and sensor survey models to assess the extent to which personal exposure signatures reflect stable urban environmental gradients. This approach allowed for the identification of fine-scale spatial variability and potential exposure hotspots not identified by long-term data sources.

To assess the urban thermal environment, we compared Landsat 8-9 OLI/TIRS Collection 2 Level 2 satellite imagery to wearable sensor data. The land surface temperature satellite data consisted of 41 images taken between May 1 and September 30, 2023. Following a Manhattan-specific clip and a standard cloud/shadow mask, each scene was centered by subtracting the island-wide median temperature from every pixel. Images were spatially aligned and averaged

across all timepoints, and the resulting mean deviation raster was smoothed using a 15x15 pixel moving window focal mean.

Personal wet bulb temperature exposure maps were generated by aggregating runner sensor measurements to 0.001° grids. To isolate spatial variability from the temporal drift occurring during each run event, we subtracted a reference value interpolated from the sensor-measured temperatures at the common start, water break, and end points. Final spatial deviations were averaged across all participants per time-indexed grid cell.

Ambient particulate matter gradients were assessed using the 2023 New York City Community Air Survey (NYCCAS) $PM_{2.5}$ regression models clipped to the Manhattan study area. Measured $PM_{2.5}$ by runner ($\mu g * m^{-3}$) were averaged to the 0.001° grid level and reported as a percentage deviation from each specific run event's average to control for day-to-day fluctuations in baseline air quality.

Statistical Analysis

Differences in environmental exposures and physiological metrics across chronological run events (R01, R02, and R03) were assessed using Friedman tests to check for consistent within-participant trends or systematic drift over time. To isolate spatial variations across run segments, linear mixed-effects models (LMEs) were used, clustered by participant identity. For analyses with multiple data points per run event, specifically segment-level profiles (Early 10-km v. Late 10-km) and built environment comparisons, the models utilized nested random intercepts to cluster on individual run events. Pairwise post-hoc comparisons were evaluated using estimated marginal means with a Tukey-Kramer adjustment for multiple comparisons. Differences in physiological and environmental exposures by sex were evaluated across all runs using an LME clustered on participant identity via a single random intercept. Age-based associations were assessed via univariate linear mixed-effects regression. All p-values from LMEs were adjusted for multiple hypothesis testing using Benjamini-Hochberg (BH) correction.

Urinary biomarker concentrations were normalized using urine spot creatinine to account for dilution. Urinary creatinine measurements reported as greater than 4 $g * L^{-1}$ were treated as right-censored at the upper quantification threshold. For primary analyses, censored values were replaced with 4.01 $g * L^{-1}$ to retain participants in the dataset. Sensitivity analyses subsequently used an alternative substitution framework at $4\sqrt{2}\ g * L^{-1}$ to assess the impact of censoring on biomarker distributions.

Within-participant biomarker comparisons from baseline to post-run were evaluated using Friedman tests and post-hoc paired Wilcoxon signed-rank tests with BH correction. To model the biological impacts of environmental and physiological exposures, LMEs with a random intercept for participant identity were used to assess within-participant associations between post-run kidney biomarkers and run-aggregated exposure metrics, adjusting for baseline biomarker levels. Residual diagnostics (Quantile-Quantile plots and Shapiro-Wilk tests) were evaluated to ensure

compliance with normality and homoscedasticity assumptions. To evaluate potential multicollinearity among exposure variables prior to WQS mixture modeling, Spearman correlation coefficients were calculated and assessed for statistical significance.

Weighted Quantile Sum Regression

To address the inherent collinearity among physiological, environmental, and performance-related metrics, a mixed-effects weighted quantile sum (WQS) regression was implemented to evaluate joint effects of the overall exposure mixture on changes in kidney biomarkers relative to baseline. WQS regression employs a unidirectional weighted index of highly collinear co-exposures to evaluate their collective association with a health outcome, ranking individual mixture components based on their relative importance [26]. The mixed-effects extension leverages this framework to assess the overall exposure mixture while also accounting for within-participant correlation across repeated running events via a participant-based random intercept [27].

Changes in all selected biomarkers were assessed using whole-run aggregated exposures as mixture components. To evaluate temporal heterogeneity within individual run events, segment-specific (Early vs. Late) exposure aggregates were additionally evaluated against biomarker changes using separate WQS mixtures.

We utilized a repeated holdout framework consisting of 30 independent iterations to estimate exposure weights and evaluate model significance. For each holdout, run events were randomly assigned to training and validation subsets using a 50/50 split, maintaining a balanced ratio of observations by sex across both subsets. Exposure variables from these training observations were transformed into quartiles to balance robustness and statistical stability given our sample size. Within the training set of a single holdout, 200 bootstrap samples were generated, and mixture component weights were estimated for each sample via nonlinear optimization constrained to a positive direction of association with the outcome. These 200 bootstrap weight vectors were then averaged to yield a single mixture composition unique to that holdout. This specific weight vector was multiplied by the exposure quartile ranks of the validation set to calculate its corresponding WQS index, which was subsequently regressed against biomarker changes to evaluate statistical significance.

This process was repeated across all 30 holdouts, resulting in 30 distinct training/validation splits, validation-set WQS indices, and regression coefficients. For final interpretation, the bootstrap-aggregated mixture weights were averaged across all 30 repeated holdouts, while the final validation regression coefficients were evaluated for statistical significance using their empirical 95% intervals across the holdouts. All model iterations were stratified by sex, with a sex to WQS index interaction term and scaled participant age included as a covariate. Mixture components whose weight surpassed the equal weight threshold across components and strata were considered significant contributors to the overall mixture effect, defined via Equation 2:

$$Threshold = \frac{1}{c \times s} \quad \textbf{(Eq. 2)}$$

Where c represents the total number of environmental and physiological variables included in the mixture, and s represents the number of categorical groupings (e.g., sex) used for weight estimation. The mixed-effects extension of WQS adjusts each holdout's regression coefficients by including a participant-based random effect term. Adjusted coefficients were statistically significant if their empirical 95% interval did not include 0 across the 30 repeated holdouts. Analyses were performed using gWQS package (version 3.0.5) in R (version 4.2.0; Vienna, Austria).

Results

Study Participants

Nineteen participants enrolled in the study, with 10 males and nine females completing at least one run from May 1, 2023 until September 30, 2023 for a total of 52 run observations (Table 1). Runners were excluded from further analysis if they did not complete all three runs (n=4) due to scheduling conflicts, injury, or deviation from the pre-defined run route by over 1-km across multiple run events (n=1). The final cohort consisted of 14 runners, 7 men and 7 women, each completing three runs for a total of 42 run observations.

Male runners were on average 2.4 years older than females. Males were primarily comprised by White participants while females were primarily Asian. Males were also taller, heavier, and ran faster than females on average.

Table 1. Cohort descriptive statistics.

	All Runners	Final Cohort	Male	Female
Count	19	14	7	7
Age (Mean, SD)	35.5 ± 10.5	37.5 ± 11.4	38.7 ± 10.1	36.3 ± 13.4
Ethnicity	White – n=8 Asian – n=9 Black – n=1 Hispanic – n=1	White – n=5 Asian – n=7 Black – n=1 Hispanic – n=1	White – n=4 Asian – n=1 Black – n=1 Hispanic – n=1	White – n=1 Asian – n=6
Height (cm)	171.3 ± 7.6	169.9 ± 7.1	174.9 ± 4.5	164.9 ± 5.5
Weight (kg)	62.9 ± 9.8	61.9 ± 10.4	70.4 ± 4.5	53.4 ± 6.6
Heart Rate (bpm) *	153.8 ± 11.7	153.5 ± 11.0	152.1 ± 12.2	154.9 ± 9.9
Speed (km/hr) *	11.4 ± 1.9	11.5 ± 2.0	12.8 ± 1.7	10.2 ± 1.1

*Average over run events

Kidney Injury Biomarker Responses

Median measured concentrations for all biomarkers increased sharply following the first run event (Figure 1A). After this, IL-18, KIM-1, YKL-40, and serum creatinine followed similar trends, with a near return to baseline following the second run and a modest increase after the

third. In contrast, MCP-1 and urine creatinine had a partial return to baseline after the second run event, with a continued decline following the third. After controlling for dilution via urine creatinine normalization, these fluctuations diminished, suggesting dehydration levels impacted measured concentrations (Figure 1B). This revealed a consistent pattern of increasing IL-18 across run events, while KIM-1, MCP-1, and YKL-40 showed similar trends between normalized and raw concentrations. Friedman tests demonstrated statistically significant overall shifts across sampling events for serum creatinine, urine spot creatinine, normalized IL-18, and normalized KIM-1 (all $p < 0.05$). In contrast, normalized MCP-1 and YKL-40 did not exhibit significant overall temporal variation across repeated samples ($p > 0.05$). Post-hoc paired Wilcoxon signed-rank tests with BH correction revealed a significant difference between baseline serum creatinine and post-run concentrations at all timepoints (all $p \approx 0.003$). Normalized IL-18 and KIM-1 showed significant elevations for participants' second and third run events relative to baseline (all $p < 0.05$). For urine creatinine, no individual pairwise comparison retained statistical significance following BH correction (all $p > 0.05$).

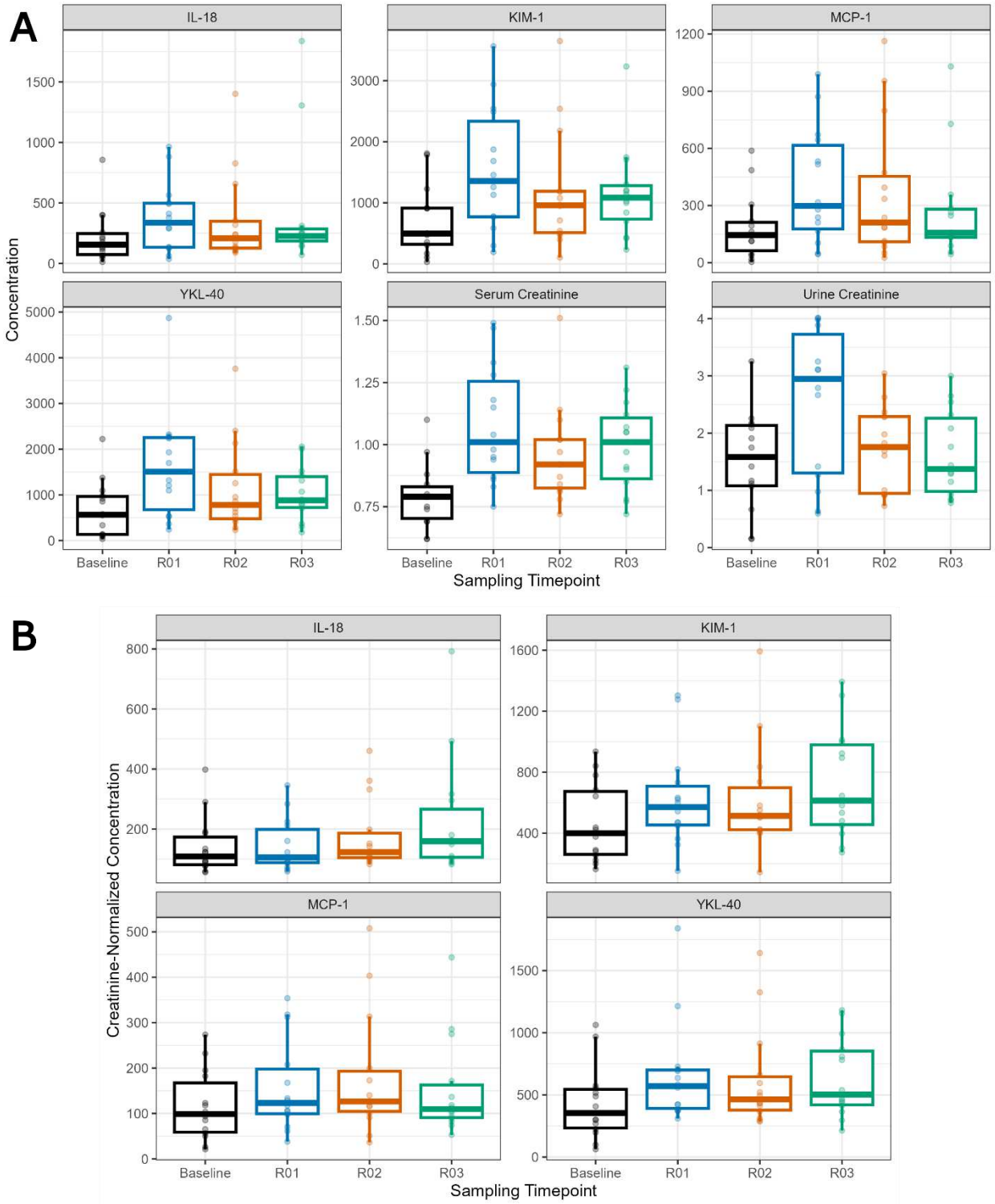


Figure 1. Panel A: Distributions of raw concentrations of novel kidney biomarkers, serum creatinine, and urine creatinine across run trials and baseline samples. Panel B: Urine creatinine-normalized novel kidney biomarker concentrations.

Because raw biomarker concentrations are sensitive to hydration levels at the time of urine sampling, subsequent analyses focused on creatinine-normalized biomarkers. For observations with censored urine creatinine measurements, $4.01\ g * L^{-1}$ was used to normalize kidney biomarker concentrations in all further analyses. Alternative censoring of $4\sqrt{2}\ g * L^{-1}$ yielded no significant difference in normalized concentrations across participants for any biomarker (all $p > 0.05$).

Similarly, the effect of hydration is evidenced by serum creatinine, which was positively correlated with estimated water loss ($r = 0.494, p = 0.0008$). Fourteen runs across eight participants had serum creatinine increases of $\geq 0.3\ mg * dL^{-1}$ relative to baseline, corresponding to Acute Kidney Injury Network (AKIN) criteria thresholds for Stage 1 AKI [28]. Paired Wilcoxon rank-sum tests showed a statistically significant difference in post-run concentrations vs. baseline for normalized IL-18, normalized KIM-1, and serum creatinine (all $p < 0.05$), whereas other biomarkers did not differ significantly.

Sex-stratified distributions revealed greater variability in normalized MCP-1 among female participants compared to males (Figure S2), though median post-run shifts were observed in both groups. Linear mixed-effects models (LMEs) showed no statistically significant difference in post-run biomarkers between male and female participants. Males exhibited higher serum creatinine and urinary IL-18 and KIM-1 changes than females ($\beta = 0.11, 0.12, 0.24$, respectively, all $p > 0.1$). Conversely, females exhibited higher MCP-1 and YKL-40 changes than males ($\beta = -0.44$ and -0.26, respectively, all $p > 0.5$).

LMEs adjusting for repeated run events within participants demonstrated no statistically significant associations between creatinine-normalized urinary biomarker responses and any whole-run environmental or physiological exposure metrics. Conversely, post-run serum creatinine percent change exhibited significant positive associations with internal markers of exertion and physiological strain, including minute ventilation, running speed, estimated water loss, and sweat rate (all $p < 0.05$).

Whole-Run Spatiotemporal Exposure Profiles

Environmental exposures showed variability across repeated run events (Figure S3). Median $PM_{2.5}$ concentration and total inhaled mass fell from Run 1 (R01) to Run 3 (R03). Across all run observations, runners were exposed to a median UPAS optical sensor-derived $PM_{2.5}$ concentration of 11.0 $\mu g * m^{-3}$ (1.2 - 48.6 $\mu g * m^{-3}$.). Median inhaled mass of $PM_{2.5}$ was 102.6 μg (12.1-591.3 μg). Wet bulb temperature distributions also declined across run events, though median exposures were relatively consistent at 20.9 $°C$ (9.5-25.0 $°C$). In contrast, physiological measures including core temperature, heart rate, minute ventilation, and sweat rate had largely overlapping distributions across run events. Running speed was also stable across sequential runs within participant. Friedman tests confirmed no statistically significant differences in

physiological or environmental exposure by run index, indicating the absence of systematic shifts across the study period.

Whole-run exposure distributions were stratified by sex (Figure 2). LMEs adjusting for repeated individual run events revealed that male participants exhibited significantly higher minute ventilation, running speed, sweat rate, and water loss compared to female participants ($p = 0.035, 0.034, 0.035, 0.038$, respectively, adjusted for multiple hypothesis testing via Benjamini-Hochberg adjustment). Core temperature was slightly higher for females, though not statistically significant ($p = 0.21$). Heart rate was comparable between the sexes ($p = 0.70$). Air and wet bulb temperature exposures also did not differ significantly between men and women ($p = 0.54$ and $p = 0.66$, respectively).

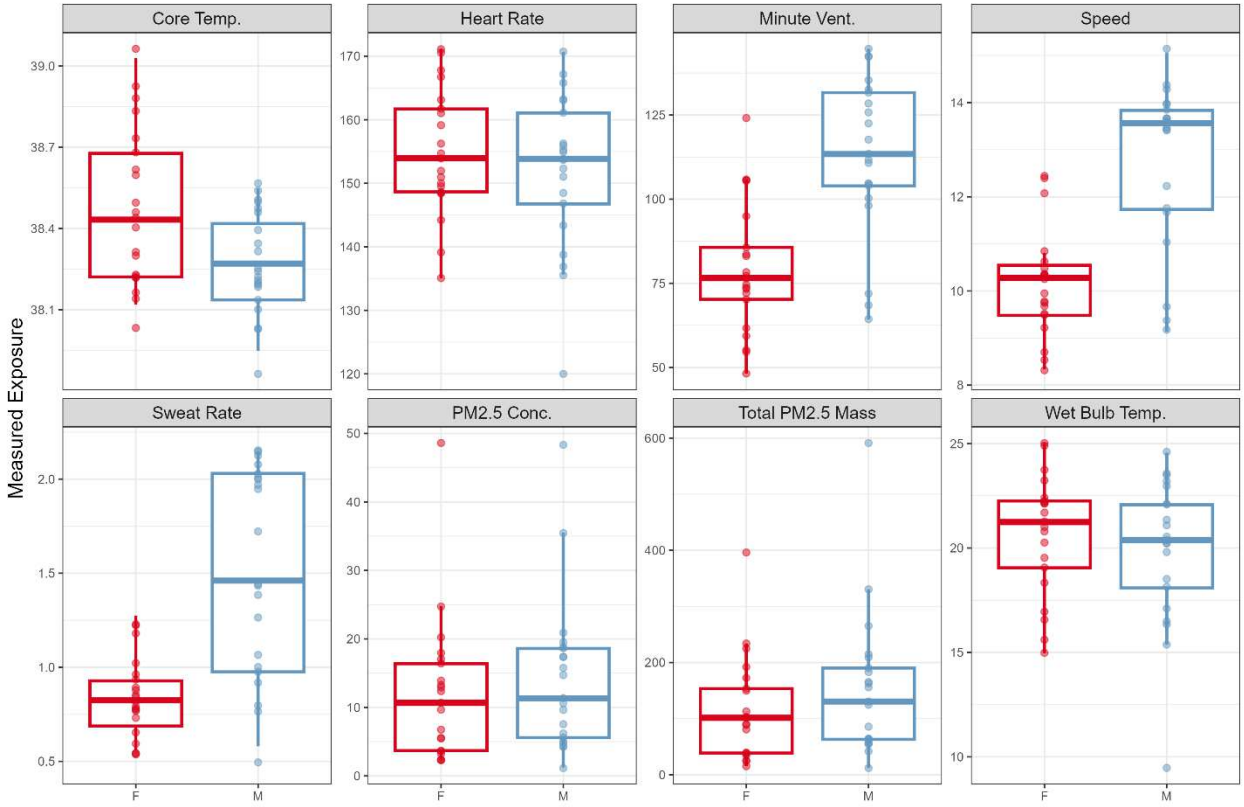


Figure 2. Sex-stratified distributions of run-aggregated thermal, physiological, and particulate exposures across run trials.

LMEs comparing particulate matter exposures ($PM_{2.5}$ concentration and inhaled mass) consistently yielded singular fits due to near-zero variance at the individual participant level. To accommodate for this, run event-specific particulate matter exposures were aggregated to a participant mean and compared between male and female participants using a Wilcoxon rank-sum test, which indicated there was no significant difference in $PM_{2.5}$ concentration of exposure

($p = 0.45$) or $PM_{2.5}$ inhaled mass of exposure ($p = 0.38$) between men and women. Univariate linear mixed-effects models indicated participant age was not significantly associated with any whole-run environmental or physiological metric when adjusted for multiple hypothesis testing (all $p > 0.83$).

Early- and Late-Run Exposure Profiles

Exposure distributions were stratified by run segment, comparing the first 10-km (Early) to the second 10-km (Late) (Figure S4). LMEs comparing segment-aggregated exposures indicated core temperature was significantly higher during the Late phase relative to Early ($p < 0.0001$), with a median increase of approximately 0.58 $°C$. Heart rate similarly increased from the Early to the Late phase ($p < 0.0001$). Other physiological measures, including minute ventilation and running speed, did not differ significantly between the two run segments ($p = 0.12$ and 0.34, respectively).

Particulate matter exposures were consistent between the Early and Late segments, showing no significant shifts in average $PM_{2.5}$ concentration ($p = 0.59$) or inhaled $PM_{2.5}$ mass ($p = 0.65$). Air temperature ($p < 0.0001$) and wet bulb temperature ($p = 0.011$) were both significantly higher in the Late phase.

Built Environment and Fine-Scale Exposure Patterns

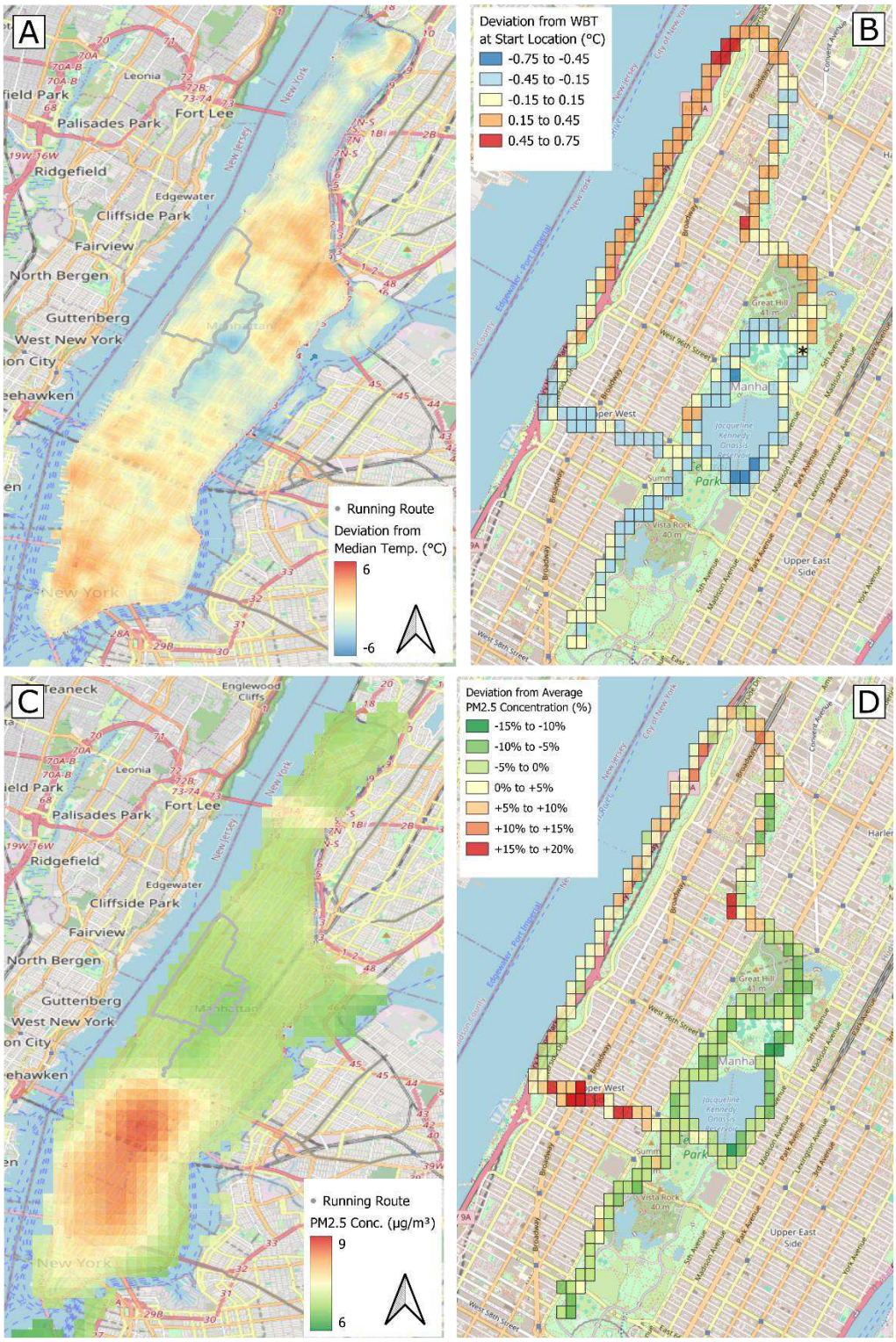
Exposure summaries across the three built environments (Park/Green Space, Bike Path, and Urban Streets) demonstrated spatial variability in both environmental and physiological metrics (Figure S5). Nested LMEs revealed significant spatial variations in heart rate, running speed, and minute ventilation. All three metrics were highest along the Bike Path, followed by the Park and were lowest within the Urban Streets. Pairwise post-hoc comparisons indicated that participants had higher heart rates on the Bike Path than the Park and Urban Street segments ($p < 0.0001$), with no significant difference between Park and Urban ($p = 0.66$). Minute ventilation and running speed were higher in both the Bike Path and Park than in the Urban Streets ($p < 0.001$). Core temperatures were significantly elevated along both the Bike Path and Urban Streets relative to Parks ($p < 0.0001$).

Environmental LMEs revealed that while ambient air temperature was not significantly different across the built environments, wet bulb temperature was significantly higher along the Bike Path than within other regions (Bike Path v. Park: $\beta = 0.42\ °C,\ p = 0.0008$, Bike Path v. Urban: $\beta = 0.28\ °C,\ p = 0.04$). In contrast, particulate matter exposures remained consistent across built environments, yielding no statistically significant differences for average $PM_{2.5}$ concentration (all $p > 0.1$).

While physiological metrics began to stabilize following the initial ramp-up phase, fine-scale aggregation to 0.001° grid cells suggested that this transition differed by sex. The grid-index profiles (Figure S6) indicated that while female participants reached a relative plateau in core

temperature, heart rate, and minute ventilation after grid index 127, corresponding to ~10-km into the run male participants showed a continued, gradual increase in these metrics through the remainder of the run. High-resolution spatial maps (Figure 3) illustrated baseline thermal and air pollution exposure gradients within Manhattan and their difference from acute personal environmental exposures. For temperature, WBT deviations were aligned with Landsat-averaged spatial trends, particularly within Central Park. A notable divergence occurred along the West Side Highway, where personal sensors recorded higher temperatures relative to the temporal reference, while satellite-derived values were below Manhattan median temperatures. (Figure 3, Panels A and B)

Air quality maps showed similar concordance, with both participant sensor-derived $PM_{2.5}$ deviations and NYCCAS estimates identifying Central Park as a low-exposure zone relative to the city streets, Upper West Side and Midtown (Figure 3, Panels C and D). Despite localized hotspots, median exposures remained within a narrow range across grid cells.



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458 **Figure 3.** Spatial comparison of environmental exposures. Panel A: Landsat-derived surface
459 temperature deviations; Panel B: Participant-derived wet bulb temperature (WBT) deviations
460 from start-point reference (denoted by *); Panel C: NYCCAS annual average $PM_{2.5}$
461 concentrations; Panel D: Participant-derived $PM_{2.5}$ percent deviations from trial mean.

WQS Regression

Sex-stratified WQS models were used to evaluate the joint association between environmental/physiological exposures and creatinine-normalized kidney biomarkers. Models specified exposure mixtures consisting of wet bulb temperature, inhaled mass of $PM_{2.5}$, core temperature, heart rate, minute ventilation, and running speed. Prior to modeling, Spearman correlation analyses revealed positive correlations between biomarker expression and primary physiological and environmental exposures (Figure S7). WQS models were thus constrained to a positive association between the exposure mixture and biomarker outcomes.

Whole-Run WQS

The WQS index (representing the effect of the exposure mixture on the outcome) was not significantly associated with serum creatinine percent change (β = 0.115, 95% CI: -0.014 - 0.244). Although several physiological exposures exceeded the equal-weight threshold, confidence intervals for the overall mixture effect included zero (Figure 4A). Extending this model, linear mixed-effects estimation was used to account for within-participant correlation across repeated runs. The WQS index remained non-significant, while age demonstrated a significant positive association with creatinine percent change (95% CI: 0.008 - 0.094).

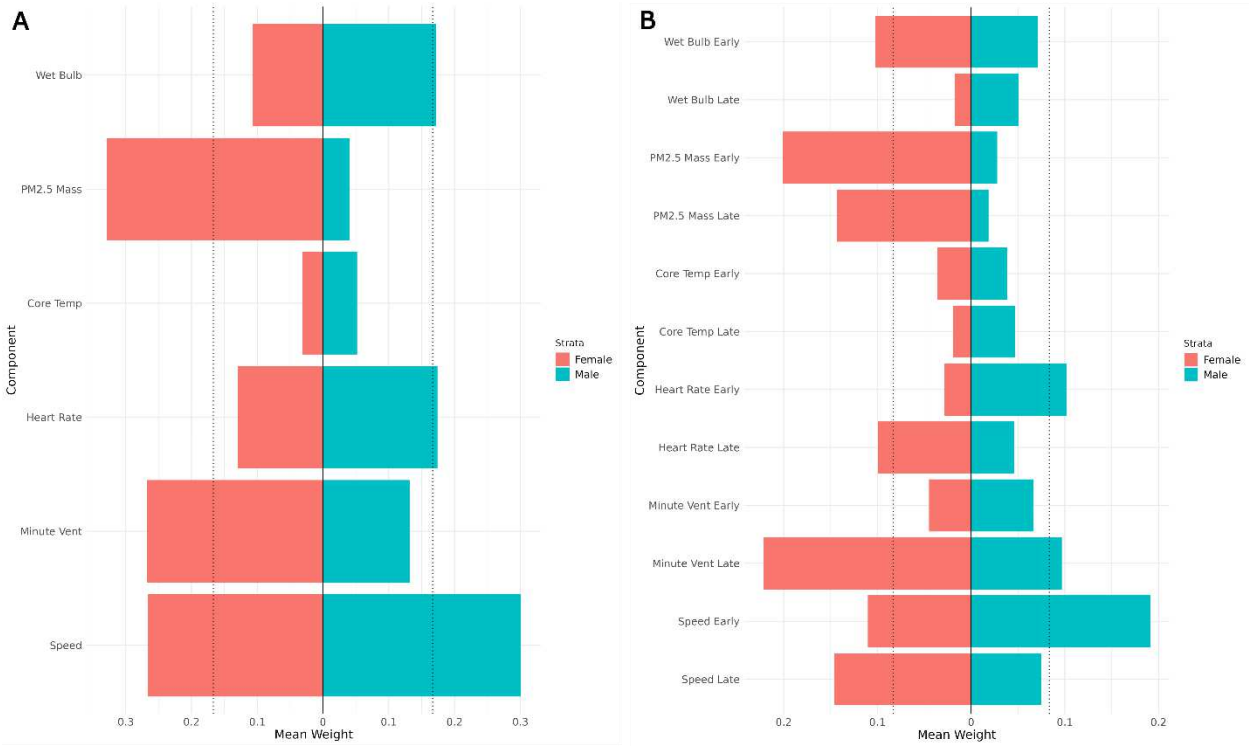


Figure 4. Average sex-stratified WQS mixture composition environmental and physiological metrics associated with increased percent change in serum creatinine relative to baseline. Panel A: Whole run-aggregated exposures. Panel B: 10-kilometer run-segment (Early and Late) aggregated exposures.

The WQS index was also not significantly associated with urinary IL-18 percent change (β = 0.467, 95% CI: -0.814 - 1.748). Weight contributions were primarily distributed across speed and heart rate, with both variables exceeding the equal-weight threshold (Figure 5A). Mixed-effects estimation did not materially alter these findings.

For urinary KIM-1 percent change, the WQS index was not statistically significant (β = 0.214, 95% CI: -0.374 - 0.802). However, male sex was significantly associated with higher KIM-1 percent change (β = 0.796, 95% CI: 0.073 - 1.520). Weight contributions were high across all variables for females, except speed and heart rate, which were higher in males (Figure 5B). Mixed-effects estimation yielded similar results.

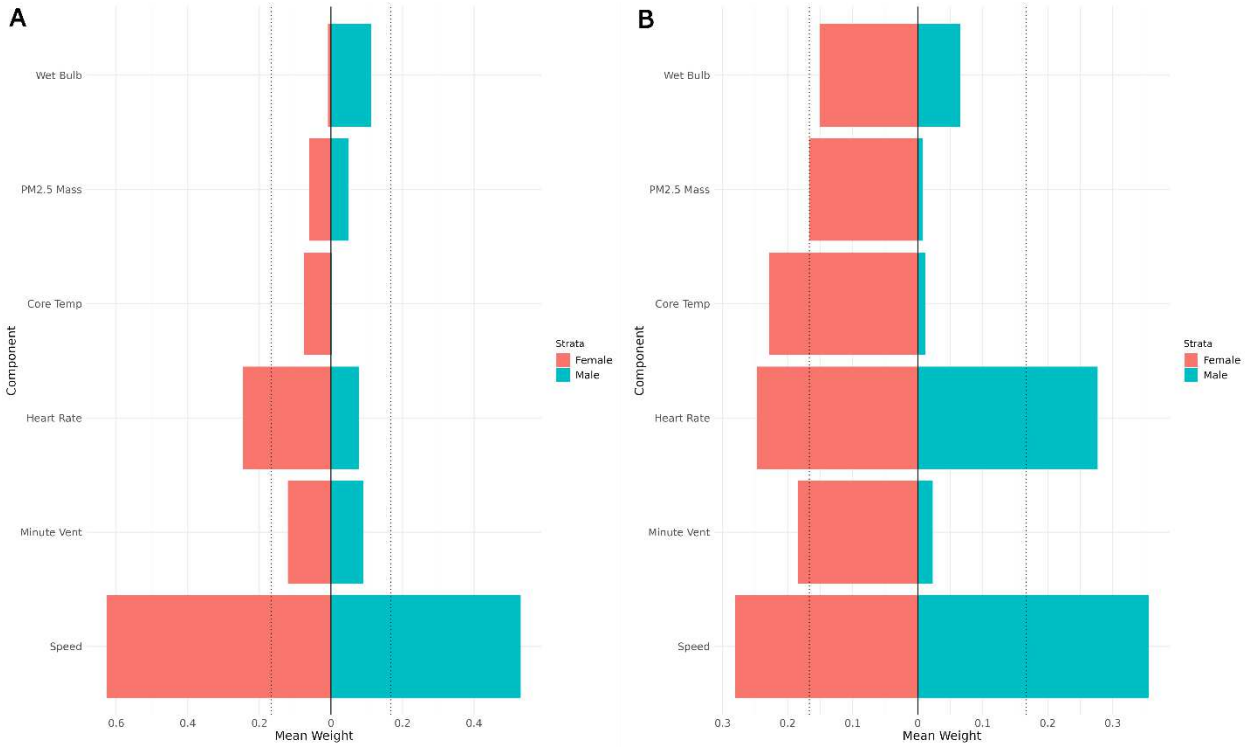


Figure 5. Average sex-stratified WQS mixture composition of whole-run aggregated environmental and physiological metrics associated with increased percent change in creatinine normalized concentrations of urinary IL-18 (Panel A) and urinary KIM-1 (Panel B) relative to baseline.

WQS models using whole-run aggregated exposures did not converge for MCP-1 or YKL-40 outcomes and were therefore not included in the final analysis.

10-km Early vs. Late-Run Segment WQS

We performed WQS regression using Early- and Late-run exposure profiles to evaluate the association of temporal variability in exposures with changes in biomarker concentrations.

In contrast to whole-run models, models including 10-km-segment exposures demonstrated significant associations between the WQS index and serum creatinine percent change (β = 0.121, 95% CI: 0.004 - 0.239). Age was also significantly associated with higher serum creatinine change (β = 0.049, 95% CI: 0.002 - 0.096).

For female participants, mixture weight contributions included Early wet bulb temperature, running speed and $PM_{2.5}$ mass in both Early and Late segments, Late heart rate, and Late minute ventilation (Figure 4B). For males, Early heart rate and speed, and Late minute ventilation surpassed the equal-weight threshold. Associations remained statistically significant following linear mixed-effects estimation, accounting for within-participant correlation.

WQS models using exposures derived from 10-km run segments did not converge for IL-18, KIM-1, MCP-1, or YKL-40 outcomes and were therefore not included in the final analysis.

Discussion

In this repeated-measures field study, we evaluated joint associations between external environmental exposures and internal physiological responses while running in a natural environment to understand kidney function, comparing high-frequency sensor data and biological sampling. Aggregate 20-km run environmental exposures were not significantly associated with post-run serum creatinine or normalized kidney biomarkers of tubular damage. Localized exposure profiles during Early- and Late-stage 10-km running windows revealed significant associations with serum creatinine percent changes, with measures of physiological strain consistently contributing more strongly to mixture weights than environmental variables. Acute post-exercise increases in kidney stress metrics were observed, with 14 runs yielding a $\geq$ 0.3 $mg * dL^{-1}$increase in serum creatinine relative to baseline, corresponding to the AKIN criteria threshold for Stage 1 AKI [28].

Analysis with linear mixed-effects models (LMEs) suggested that the observed environmental exposures were not significantly associated with the normalized urine biomarkers or serum creatinine. However, changes in serum creatinine were associated with internal physiological metrics, including water loss, sweat rate, running speed, and minute ventilation all of which are influenced by environmental exposures. Contrasting the run events where runners reached Stage 1 AKI revealed that significantly differentiating exposures were limited to markers of internal physiological strain, specifically water loss and average heart rate. Both dehydration and elevated cardiovascular workload have been shown to harm the kidneys via reduced renal perfusion [29, 30]. Despite this, LMEs showed no statistically significant differences in the normalized changes in kidney biomarkers (IL-18, KIM-1, MCP-1, and YKL-40) between the two groups at this distance. This suggests that changes in creatinine following training runs of approximately 90 to 120 minutes in summer urban environmental conditions may reflect hemodynamic stress rather than structural injury. These findings suggest that internal physiological strain plays a larger role in short-term kidney stress than fluctuations in wet bulb

temperature or particulate matter exposure alone during one training run, though their presence in WQS mixture models may suggest an additive effect. Furthermore, temporal resolution of exposure aggregation appears to be critical; aggregating exposures over large temporal and spatial periods may obscure associations that emerge when physiological stress builds over time.

Comparing long-term estimates of $PM_{2.5}$ and temperature with sensor-captured data (Figure 3) identifies specific high-exposure areas of concern across Manhattan, driven by the interaction of the local built environment with regional air masses. A primary area of concern lies within the Upper West Side and Midtown: high-density buildings and urban canyons restrict airflow, creating localized exposure traps of particulate matter exacerbated by construction- and traffic-related emissions, while concrete and asphalt surfaces absorb solar radiation, increasing local temperatures. Conversely, large vegetative zones like Central Park exhibit a microclimatic buffer effect. Improved airflow and canopy-driven particulate deposition reduce local $PM_{2.5}$ concentrations, while evapotranspiration and shading lower air temperatures.

Landsat models show the West Side Highway corridor as a cooler zone, while our wearable sensors recorded elevated wet bulb temperatures along this portion, driven by direct solar radiation and heat reflecting off large stretches of unshaded asphalt. This divergence shows that satellite-derived data can underestimate the localized thermal strain experienced by an exercising athlete, reinforcing the value of personal measurement over regional models.

To account for cross-sectional differences between static satellite imagery and real-time personal tracking, personal exposures were temporally adjusted by the temperature at the starting location, measured at three distinct timepoints during the run. Even so, runners consistently experienced higher ambient temperatures during the Late 10-km phase, reflecting both a natural diurnal warming trend – as many runs began in early morning – and the built environment, since Late-run segments systematically recorded higher temperatures than concurrent Park exposures.

In our evaluation of the physiological response to running under urban environmental conditions, distinct patterns emerged between male and female participants. Males consistently maintained higher average running speeds, sweat rates, and minute ventilation rates, while female runners showed higher baseline and peak internal body temperatures (Figure S6). These variations may partially be explained by differences in our cohort's background running experience, as the male sub-cohort was largely composed of former collegiate runners, while the female sub-cohort consisted of two former collegiate runners and five recreational runners. Consequently, the descriptive differences observed in our cohort likely reflect a combination of baseline athletic experience and inherent biological variations in sex-specific responses to endurance running. To isolate these factors, our modeling framework explicitly attempted to account for training status and baseline fitness differences by clustering repeated run events within-participant. These baseline differences align with established literature on sex differences in thermoregulation: women frequently exhibit a lower sweating capacity and a higher sweating-onset temperature threshold than men, promoting greater heat storage during prolonged exercise [31].

Sex-related differences were also observed in kidney biomarker trends, though largely descriptive. Male runners demonstrated larger post-run increases in serum creatinine, comprising the majority (11/14) of the run events that met the AKIN criteria for Stage 1 AKI. Unadjusted comparisons showed IL-18 and KIM-1 changes were nominally higher in men with MCP-1 and YKL-40 nominally higher in women, though none were statistically significant (all $p > 0.1$). However, in the sex-stratified WQS mixture models, male sex was significantly associated with higher KIM-1 percent change (β = 0.796, 95% CI: 0.073 - 1.520). This pattern is potentially consistent with males showing greater susceptibility to glomerular hyperfiltration and tubular strain under acute physiological stress (van Eeghen, Pyle et al. 2025, Neugarten and Golestaneh 2013)

The WQS models examining post-run serum creatinine changes revealed distinct, descriptive patterns in the exposure mixture weights between sexes. For male runners, the overall mixture effect was predominantly weighted toward internal physiological metrics, specifically speed and heart rate during the Early 10-km phase and minute ventilation during the Late phase, consistent with high-intensity effort driving transient renal hypoperfusion and a compensatory drop in glomerular filtration [32, 33]. However, because the male sub-cohort maintained faster paces at comparable heart rates, this heavy internal mixture weight may simply reflect higher absolute workload rather than an inherent sex-specific difference. Conversely, the female exposure mixture demonstrated a proportionally greater contribution from external environmental components, particularly inhaled $PM_{2.5}$ mass of exposure, consistent with prior evidence of stronger $PM_{2.5}$-associated cardiovascular and inflammatory responses in women [34, 35].

While the models isolating Early- versus Late-run dynamics revealed these descriptive shifts, our primary 20-km run-aggregated models evaluating whole-run exposures showed no significant associations with any post-run kidney biomarker outcome. This discrepancy suggests that whole-run aggregated exposures may lack the necessary temporal granularity to capture acute biological responses and highlights that explicit stratification by sex and granular, time-resolved exposure metrics will be critical for interpreting multi-exposure dynamics in future, larger-scale athletic cohorts.

Strengths and Limitations

A primary strength of this study is the integration of high-frequency environmental and physiological monitoring via personal wearable sensors with repeated biological sampling in a real-world, outdoor exercise environment. By utilizing a repeated-measures design where each participant's run events were clustered, we were able to account for baseline fitness variations and training status. This granular approach, paired with sex-stratified Weighted Quantile Sum (WQS) mixture modeling and linear mixed-effects estimation allowed for the analysis of rich, multi-faceted data of co-occurring environmental and internal stressors. Furthermore, utilizing fine-scale spatial aggregation empowered the identification of localized exposure patterns that regional macro-level models systematically overlook.

Despite these methodological strengths, several limitations must be acknowledged. First, as an exploratory pilot study, our sample size of runners was small, with 14 participants completing three run events each for a total of 42 observations, reducing our statistical power. Furthermore, evaluating the independent relationships of a wide array of environmental and physiological exposures against the same biological outcomes inflated our risk of Type I error due to multiple hypothesis testing. This limitation likely contributed to our null whole-run aggregated exposure WQS models and underscores that our findings should be interpreted as hypothesis-generating. Additionally, our cohort was predominantly composed of White and Asian individuals, which limits the generalizability of these findings to more diverse populations. Future studies should prioritize larger, demographically diverse cohorts to investigate potential subgroup differences.

Second, real-world deployment of personal monitoring equipment introduces technical and operator challenges. High-frequency wearable sensor measurements are inherently subject to instrument noise, occasional data gaps, and potential electronic interference within high-density urban environments. Because of localized sensor dropouts or technical malfunction during field deployment, certain secondary sensor measures had to be substituted to maintain data continuity. Human and operator error in the field also presented challenges, particularly regarding the logistics of biological sample processing. An unexpected change in sample freezer allocation required the physical transfer of biological specimens, introducing an ethical and analytical risk of sample degradation or contamination during the relocation process.

Finally, our analytical framework carried inherent statistical assumptions. While creatinine normalization was necessary to ensure comparability across subjects and fluctuating hydration levels, right-censored substitutions for urinary creatinine values above the limit of detection introduced additional uncertainty. Furthermore, WQS regression assumes a unidirectional association between exposure mixture components and outcomes, reducing its ability to detect opposing effects.

Future Extensions and Applications

This study provided a framework for capturing natural environmental exposures at high spatial and temporal resolution. Our design included lightweight wearable sensors to capture personal exposures while minimizing the burden of monitoring equipment on participants' running performance. This study design and methodology is appropriate to expand from runners to occupational settings where kidney health associated with heat or air pollution exposure is of concern [36].

From a practical standpoint, understanding the relationship between environmental exposures and intensity of exertion can inform guidance for recreational runners, athletes, and outdoor workers. Incorporating physiological monitoring into environmental health research may enhance risk assessment of climate-driven changes in heat and air quality on human health.

Contributors

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Role of the funding source

The funders of this study had no role in the study design, data collection, data analysis, data interpretation, or writing of this report.

Declaration of interests

The authors have declared that no competing interests exist.

Data sharing

Data will be made available on request.

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References:

1. Luber, G. and M. McGeehin, *Climate change and extreme heat events.* American journal of preventive medicine, 2008. **35**(5): p. 429-435.
2. Currie, J. and R. Walker, *What do economists have to say about the Clean Air Act 50 years after the establishment of the Environmental Protection Agency?* Journal of Economic Perspectives, 2019. **33**(4): p. 3-26.
3. Clay, K., N.Z. Muller, and X. Wang, *Recent increases in air pollution: evidence and implications for mortality.* Review of Environmental Economics and Policy, 2021. **15**(1): p. 154-162.
4. Burke, M., et al., *The contribution of wildfire to PM2. 5 trends in the USA.* Nature, 2023. **622**(7984): p. 761-766.
5. Zhang, M., et al., *Wildfire smoke PM2. 5 and mortality rate in the contiguous United States: A causal modeling study.* Science Advances, 2026. **12**(6): p. eadw5890.
6. Chen, J. and G. Hoek, *Long-term exposure to PM and all-cause and cause-specific mortality: a systematic review and meta-analysis.* Environment international, 2020. **143**: p. 105974.
7. Afsar, B., et al., *Air pollution and kidney disease: review of current evidence.* Clinical kidney journal, 2018. **12**(1): p. 19-32.
8. Beker, B.M., et al., *Human physiology in extreme heat and cold.* Int Arch Clin Physiol, 2018. **1**(1): p. 1-8.
9. Gonzalez, R.R., K.B. Pandolf, and A.P. Gagge, *Heat acclimation and decline in sweating during humidity transients.* Journal of Applied Physiology, 1974. **36**(4): p. 419-425.
10. Dockery, D.W. and C.A. Pope, *Acute respiratory effects of particulate air pollution.* 1994.
11. Rasking, L., et al., *Ambient black carbon reaches the kidneys.* Environ Int, 2023. **177**: p. 107997.
12. Hamanaka, R.B. and G.M. Mutlu, *Particulate Matter Air Pollution: Effects on the Cardiovascular System.* Frontiers in Endocrinology, 2018. **Volume 9 - 2018**.
13. Daigle, C.C., et al., *Ultrafine particle deposition in humans during rest and exercise.* Inhal Toxicol, 2003. **15**(6): p. 539-52.
14. Kenefick, R.W., S.N. Cheuvront, and M.N. Sawka, *Thermoregulatory Function During the Marathon.* Sports Medicine, 2007. **37**(4): p. 312-315.
15. Giles, L.V. and M.S.J.S.M. Koehle, *The health effects of exercising in air pollution.* 2014. **44**(2): p. 223-249.
16. Sanches, T.R., et al., *Air pollution aggravates renal ischaemia–reperfusion-induced acute kidney injury.* The Journal of Pathology, 2024. **263**(4-5): p. 496-507.
17. Siew, E.D., L.B. Ware, and T.A. Ikizler, *Biological Markers of Acute Kidney Injury.* Journal of the American Society of Nephrology, 2011. **22**(5): p. 810-820.
18. Madureira, J., et al., *Cardio-respiratory health effects of exposure to traffic-related air pollutants while exercising outdoors: A systematic review.* Environmental Research, 2019. **178**: p. 108647.
19. Remigio, R.V., et al., *Combined effects of air pollution and extreme heat events among ESKD patients within the Northeastern United States.* Science of The Total Environment, 2022. **812**: p. 152481.
20. Clarkson, P.M., *Exertional rhabdomyolysis and acute renal failure in marathon runners.* Sports medicine, 2007. **37**(4-5): p. 361-363.

21. DeMartini, J.K., et al., *Environmental conditions and the occurrence of exertional heat illnesses and exertional heat stroke at the Falmouth Road Race.* Journal of athletic training, 2014. **49**(4): p. 478-485.
22. Mansour, S.G., et al., *The Role of Volume Regulation and Thermoregulation in AKI during Marathon Running.* Clinical Journal of the American Society of Nephrology, 2019. **14**(9): p. 1297-1305.
23. Mansour, S.G., et al., *Kidney injury and repair biomarkers in marathon runners.* American Journal of Kidney Diseases, 2017. **70**(2): p. 252-261.
24. McCullough, P.A., et al., *Changes in renal markers and acute kidney injury after marathon running.* Nephrology, 2011. **16**(2): p. 194-199.
25. *Appendix G to Part 58—Uniform Air Quality Index (AQI) and Daily Reporting.* Code of Federal Regulations, 2020. **Title 40**(Part 58): p. Appendix G.
26. Tanner, E.M., C.-G. Bornehag, and C. Gennings, *Repeated holdout validation for weighted quantile sum regression.* MethodsX, 2019. **6**: p. 2855-2860.
27. Gennings, C., et al., *Weighted quantile sum (WQS) mixed-effects model.* MethodsX, 2025. **15**: p. 103580.
28. Mehta, R.L., et al., *Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury.* Critical Care, 2007. **11**(2): p. R31.
29. Roncal-Jimenez, C., et al., *Mechanisms by Which Dehydration May Lead to Chronic Kidney Disease.* Ann Nutr Metab, 2015. **66 Suppl 3**: p. 10-3.
30. Messina, A., et al., *Understanding fluid dynamics and renal perfusion in acute kidney injury management.* J Clin Monit Comput, 2025. **39**(1): p. 73-83.
31. Costa, J.G., et al., *Sex differences in the thermoregulatory and cardiovascular response to exercise in hot environmental conditions.* American Journal of Physiology-Regulatory, Integrative and Comparative Physiology, 2025. **329**(5): p. R651-R660.
32. Brilland, B., et al., *Kidney injury molecule 1 (KIM-1): a potential biomarker of acute kidney injury and tubulointerstitial injury in patients with ANCA-glomerulonephritis.* Clin Kidney J, 2023. **16**(9): p. 1521-1533.
33. Gounden, V., H. Bhatt, and I. Jialal, *Renal Function Tests.* StatPearls, 2024.
34. Clougherty, J.E., *A growing role for gender analysis in air pollution epidemiology.* Environ Health Perspect, 2010. **118**(2): p. 167-76.
35. Rasking, L., et al., *Adverse Effects of fine particulate matter on human kidney functioning: a systematic review.* Environ Health, 2022. **21**(1): p. 24.
36. Bradley, M., et al., *A critical review of a hidden epidemic: examining the occupational and environmental risk factors of chronic kidney disease of unknown etiology (CKDu).* Environmental Science: Advances, 2025. **4**(1): p. 57-76.

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