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Authors

Chang, Howard
Zhang, Haisu
Latimore, Amanda
et al.

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Associations between short-term ambient temperature exposure and emergency department visits for amphetamine, cocaine, and opioid use in California from 2005 to 2019

Howard H. Chang[a,b,*], **Haisu Zhang**[b], **Amanda D. Latimore**[c], **Brian P. Murray**[d], **Rohan R. D'Souza**[a], **Noah Scovronick**[b], **Matthew O. Gribble**[e], **Stefanie T. Ebelt**[b]

[a]Department of Biostatistics and Bioinformatics, Emory University, Atlanta, GA, USA

[b]Gangarosa Department of Environmental Health, Emory University, Atlanta, GA, USA

[c]Center for Addiction Research and Effective Solutions, American Institutes for Research, Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

[d]Emergency Medicine, Boonshoft School of Medicine, Wright State University, Dayton, OH, USA

[e]Department of Epidemiology, University of Alabama at Birmingham, Birmingham, AL, USA

Abstract

Substance use disorder is a growing public health challenge in the United States. People who use drugs may be more vulnerable to ambient heat due to the effects of drugs on thermoregulation and their risk environment. There have been limited population-based studies of ambient temperature and drug-related morbidity. We examined short-term associations between daily ambient temperature and emergency department (ED) visits for use or overdose of amphetamine, cocaine and opioids in California during the period 2005 to 2019. Daily ZIP code-level maximum, mean, and minimum temperature exposures were derived from 1-km data Daymet products. A time-stratified case-crossover design was used to estimate cumulative non-linear associations of daily temperature for lag days 0 to 3. Stratified analyses by patient sex, race, and ethnicity were also conducted. The study included over 3.4 million drug-related ED visits. We found positive associations between daily temperature and ED visits for all outcomes examined. An increase in daily mean temperature from the 50th to the 95th percentile was associated with ED visits for amphetamine use (OR = 1.072, 95% CI: 1.058, 1.086), cocaine use (OR = 1.044, 95% CI: 1.021, 1.068 and opioid use (OR = 1.041, 95% CI: 1.025, 1.057). Stronger positive associations were also observed for overdose: amphetamine overdose (OR = 1.150, 95% CI: 1.085, 1.218), cocaine overdose (OR = 1.159, 95% CI: 1.053, 1.276), and opioid overdose (OR = 1.079, 95% CI: 1.054, 1.106). In summary, people who use stimulants and opioids may be a subpopulation sensitive

*Corresponding author at: 1518 Clifton Rd., NE Atlanta, GA 30322, USA. howard.chang@emory.edu (H.H. Chang).

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2023.108233.

to short-term higher ambient temperature. Mitigating heat exposure can be considered in harm reduction strategies in response to the substance use epidemic and global climate change.

Keywords

Substance use; Overdose stimulant; Cocaine; Opioid; Heat; Temperature

1. Introduction

Substance use disorder is a major public health challenge in the United States (US). In 2021, more than 40 million people aged 12 or older used illicit drugs, and over 107,000 drug-related overdose deaths were reported (SAMHSA, 2022a; Spencer et al. 2022). While opioid overdoses have deservedly captured national attention, the predictable shift in trend from opioids to stimulants has led to a recognition of the increasing - but less understood - role of stimulants and polysubstance use in domestic and international drug overdose trends (Black et al. 2022, Cicero et al. 2020, Jones et al. 2021, Morley et al. 2017). For example, from 2012 to 2019, the rate of death related to cocaine overdose in the US increased more than 3-fold, and deaths related to stimulants increased more than 6-fold (Hedegaard et al. 2021). Significant gaps in knowledge exist on how to best support those with stimulant use disorder (Fischer et al. 2021).

Increasingly, public health practitioners are linking structural and social determinants of health with overdose (Jalali et al., 2020; Latimore et al., 2023; American Institutes for Research, 2023). However, limited attention has been given to the physical context in which people use drugs and the intersection of climate change, the built environment, and harm reduction. High ambient temperature is considered a significant risk factor for human health, especially with the changing climate projected to have more frequent and intense extreme heat events (Armstrong et al. 2019, Guo et al. 2017, Reidmiller et al. 2019). People who use cocaine or other stimulants, such as amphetamines (e.g., methamphetamine, ecstasy), may be more sensitive to heat exposure due behavior-related risk environments (Vergunst et al. 2022), and several pathophysiological mechanisms, including altered thermoregulation, neurotoxicity and kidney injury (Kiyatkin et al. 2014, Liechti 2014, Mansoor et al. 2017).

Population-based epidemiological evidence on the health effect of heat exposure among people who use drugs is sparse. Previous studies have predominantly focused on death as the primary outcome of interest, case studies of historical heat wave events, and among people who use cocaine (Auger et al. 2017, Kilbourne 1998, Marzuk et al. 1998). While studies on heat and morbidity outcomes are increasing, they have typically only considered substance use as part of an undifferentiated definition of mental health outcomes that included those due to alcohol, cannabinoids, tobacco, and hallucinogens (Nori-Sarma et al. 2022, Yoo et al. 2021). Furthermore, identification of drug-related morbidity in administrative databases is often restricted to diagnoses classified under mental disorders. This approach may under-ascertain overdoses, which are classified as poisoning and external causes of injury.

To address these knowledge gaps, this study aims to examine short-term associations between daily ambient temperature and emergency department (ED) visits for drug-specific

use and overdose in California over a 15-year period. We focus on amphetamine, cocaine, and opioids, which are among the top five drugs involved in drug-related ED visits in the U.S., with the other two being alcohol and cannabinoids (SAMHSA, 2022b). Furthermore, because heat exposure may impact multiple organs and systems, we consider ED visits with drug-related diagnosis, including both substance use and overdose, as the outcome of interest. We chose ED visit as the measure of morbidity because EDs often serve as the safety net for treatment access in a behavioral health system that has insufficient providers and many barriers for those seeking care (Hinderaker et al. 2020). Given the structurally-driven racial disparities that exist in US drug overdoses (Ahmad et al., 2022; Han et al., 2022; Jordan et al., 2022), we explore effect modification by patient race/ethnicity and sex.

2. Methods

2.1. Emergency department Visit, meteorology and ZIP code-level covariate data

We obtained patient-level ED visits during 2005–2019 from the California Office of Statewide Health Planning and Development. The definition of an ED visit included ED patients who were discharged directly, as well as ED patients admitted to the hospital. ED records included admission date, age in years, sex, race, ethnicity, self-reported patient's residential ZIP code, and International Classification of Diseases (ICD) diagnosis codes. Both primary and secondary ICD diagnosis codes were used to identify ED visits associated with substance use and overdose for amphetamine, cocaine, and opioids. ICD codes for use and overdose were mutually exclusive and are provided in Supplementary Table S1. ED visits with both overdose and use diagnoses were defined as overdose.

Daily maximum and minimum temperature in degrees Celsius, and water vapor pressure (a measure of humidity) in pascals at 1 km × 1 km spatial resolution were acquired from Daymet Version 4 (Thornton et al. 2020). Daymet is based on observed meteorology from US automated surface observing stations, which include airports, cooperative network, and some regional mesonets, providing roughly 10–15,000 temperature observations per day across the contiguous US. Daymet has been found to accurately describe ambient temperature and mean heat index at weather stations (Thomas et al. 2021, Weinberger et al. 2019). Daily mean temperature was calculated by taking the average of daily maximum and minimum temperature. Daily 1-km gridded Daymet data were aggregated to the annual ESRI ZIP code boundary by spatial averaging. Daily apparent temperature metrics (maximum, minimum, mean) were calculated from temperature and water vapor pressure as $AT = -1.3 + 0.92\,T + 2.2e$, where AT is apparent temperature (°C), T is temperature (°C), and e is water vapor pressure (kPa) (Steadman 1984).

2.2. Statistical analyses

We used distributed lag non-linear models to estimate short-term effects of temperature on ED visits for substance use, overdose, or a combined analysis of both use and overdose. All associations were estimated using conditional logistic regression models with a case-crossover design. Specifically, a matched case-control stratum was created for each ED visit. The date of the ED visit was treated as the case, and control dates were selected as the same day-of-the-week within the same calendar month. We then assigned temperature

to each case and control dates using the patient's ZIP code. This case-crossover design automatically controls for individual-level time-invariant confounders (e.g. age, sex, race) because each person serves as their own control. In our primary analysis, we utilized unconstrained distributed lag models which simultaneously included same-day temperatures (lag 0) and temperatures from up to the previous 3 days (lag 1, lag 2 and lag 3) using conditional logistic regression and the package *dlnm* for spline basis function creation (version 2.4.7) (Gasparrini 2011). This approach aimed to flexibly capture sustained effects of temperature that may last over a few days. For each temperature metric, we summarized the cumulative effect across exposure days from the distributed lag models. The cumulative effect is defined as the sum of lag-specific log odds ratios associated with a specific temperature and the median temperature (reference exposure).

Our models also included several time-varying confounders. First, within-month residual temporal trend was controlled using either day of the year or calendar date. Second, we controlled for daily dew-point temperature using the same nonlinear distributed specification as the temperature exposure. Since dew-point temperature and apparent temperature were both computed from water vapor pressure, we did not include dew-point temperature when apparent temperature is the exposure of interest. Finally, indicators of federal holidays were included. All non-linear associations were modeled using natural cubic splines. We also explored potential effect modifications by patient sex, race, and ethnicity in stratified analysis. All data analyses were performed in R 4.0.2 (R Core Team 2022).

We considered various model specifications to evaluate the robustness of estimated associations. These included (1) varying the length of exposure lag days from 0 to 3; (2) allowing the lag exposure–response function to change linearly by lag, to be identical across different lags or to be independent across lags; (3) varying the degrees of freedom (DF) for the exposure–response function from 3 to 6; (4) modeling the temporal trend using calendar date with DF varying from 1 to 6 per year, or with day of year with DF varying from 1 to 6, (5) assuming a linear exposure-response function, and (6) restricting to only ED visits with a primary diagnosis of substance use. We report results from the model with the minimum Akaike's information criterion for each outcome. Specifications of the selected primary models for each outcome are given in Table S2.

3. Results

Table 1 gives the number of ED visits for amphetamine, cocaine and opioid use or overdose, stratified by sex, age group, and race/ethnicity. Overall, the study included over 3.4 million ED visits (1,574,162 for amphetamine, 542,457 for cocaine, and 1,293,812 for opioid). For amphetamine and cocaine ED visits, around two-third of patients were male. Patients for cocaine and opioid ED visits tended to be older. Table S3 describes the degree of polysubstance use based on codiagnoses of multiple outcomes.

Proportions of ED visits with only 1 diagnosed substance use or overdose were 86.4% for amphetamine, 73.0% for cocaine, and 86.6% for opioid. The largest portion of polysubstance ED visits was for cocaine and amphetamine (n = 85,836), representing 15.8% of cocaine-related ED visits. Table S4 gives the proportion of acute kidney injury, fluid and

electrolyte imbalance and heat illness among ED visits for drug use/overdose. We found higher proportions of these heat-sensitive outcomes for drug overdose ED visits compared to drug use.

Summary statistics of different temperature metrics across the study period in California are given in Table S5. The mean and standard deviation (SD) of daily mean, maximum, minimum temperature in Celsius degree (°C) were 16.34 (6.63), 22.70 (7.87), 9.98 (5.96), respectively. Apparent temperature had similar summary statistics with mean (SD) of 15.53 (6.27), 21.38 (7.33), 9.68 (5.74) for daily mean, maximum, minimum apparent temperature.

Fig. 1 shows the exposure-response functions for ED visits and 4-day cumulative exposure to daily mean temperature (lags 0 to 3) by use, overdose, and use or overdose. The median of daily mean temperature (16.4 °C; 61.5°C) was used as the reference exposure level. For all outcomes the odds of ED visits generally increased with increasing daily mean temperature, with larger odds ratios (ORs) observed for overdose compared to substance use outcomes. For cocaine overdose, a positive association was only observed at daily mean temperatures greater than ~ 17 °C. Point estimates and CIs are reported in Table S6. In sensitivity analyses, we found that the exposure–response function of some outcomes can be approximately by a linear relationship. For example, a per °C increase in exposure was associated with a 0.7% (95% CI: 0.6%, 0.8) increase in ED visits for amphetamine use and a 0.7% (95% CI: 0.5%, 0.9%) increase in ED visits for opioid use. Further comparisons between linear and non-linear associations are given in Supplementary Table S7.

Fig. 2 shows the ORs associated with substance-related ED visits comparing the 95th percentile and the 50th percentile of exposure with different temperature metrics. Overall, associations between daily temperature and substance-related ED visits were robust across the different temperature metrics. For daily mean temperature, a stronger association based the magnitude of OR was found for amphetamine use (OR = 1.072, 95% CI: 1.058, 1.086) compared to cocaine use (OR = 1.044, 95% CI: 1.021, 1.068) and opioid use (OR = 1.041, 95% CI: 1.025, 1.057). For overdose, stronger associations were found for amphetamine overdose (OR = 1.150, 95% CI: 1.085, 1.218) and cocaine overdose (OR = 1.156, 95% CI: 1.053, 1.276) compared to opioid overdose (OR = 1.079, 95% CI: 1.054, 1.106). We note that our models did not control for substance use when analyzing overdose; hence associations with overdose and temperature may be partially attributed to increase use. Sensitivity analyses on the exposure–response function and residual temporal trend did not meaningfully impact our findings.

Fig. 3 shows the ORs associated with substance-related ED visits comparing the 95th percentile and 50th percentile exposure of daily mean temperature stratified by our selected effect modifiers of interest. Males had higher odds ratios than females, particularly for opioid use (p-value < 0.05). For amphetamine use, associations were weaker among non-Hispanic Black patients compared to Hispanic patients (p-value < 0.05). Point estimates and CIs are reported in Table S8.

Supplementary Table S9 gives the percent of ED visits ascertained only through primary diagnosis. We found that substance use was mostly ascertained via secondary diagnosis

(87.2% for amphetamine, 93.6% for cocaine and 93.7% for opioid). While, for overdose, the diagnosis codes often occur in the primary field. When the analysis was restricted to only ED visits ascertained with primary diagnosis codes, we continue to find robust positive association for all outcomes, but with larger confidence intervals due to reduced sample size.

4. Discussion

We investigated short-term associations between daily temperature and ED visits for substance use and overdose. Based on over 3.5 million ED visits in California, as expected, we found robust positive associations between higher daily temperature and ED visits related to amphetamines and cocaine (use or overdose). Positive associations with opioid ED visits were less expected from a heat-related toxicological perspective because opioids do not have hyperthermic properties similar to stimulants. This suggests possible impacts of the environment on drug use behavior and the role of multi-substance use patterns (e.g., 13% of opioid ED visits had a co-diagnosis of amphetamine or cocaine).

There has only been a small number of population-based studies on ambient temperature and substance use morbidity. A time-series analysis in New York State reported positive associations between daily average temperature and substance use ED visits (Yoo et al. 2021). Specifically, cumulative exposure (lags 0–7) was associated with a relative risk (RR) of 1.40 (95% CI: 1.18 – 1.42) comparing exposure at the 2.5th percentile (−15.91 °C) and the 97.5th percentiles (27.07 °C). A more recent case-crossover study in New York State reported an OR of 1.034 (95% CI: 1.015, 1.054) for psychoactive substance use ED visit per interquartile range increase in average daily temperature (Deng et al. 2022). Third, a large US national study among a convenience sample of adults with private insurance, reported an incidence rate ratio of 1.08 (95% CI: 1.07–1.10) between substance use disorder ED visits and warm-season daily maximum temperature (95th percentile versus the temperature associated with the minimum ED visits) (Nori-Sarma et al. 2022).

Notably, these three previous studies used broader definitions of substance use that also included alcohol and cannabinoids. In contrast, our study examined three specific substances, where patients may be particularly sensitive to heat exposure. We also considered substance use and overdose as separate outcomes to reflect differences in severity, including diagnosis codes that fall under poisoning of psychotropic drugs (Supplementary Table S1). We were not aware of previous investigations of effect heterogeneity for substance use/overdose ED visits by subpopulations. For broad mental health ED visits, Nori-Sarma et al. (2021) found higher risks among adult men compared to woman in their national analysis, but Yoo et al. (2021) and Deng et al. (2022) did not in New York State. Our stratified analyses using substance-specific ED visits suggest that heat-related risks may differ among sub-populations defined by race/ethnicity, which may be attributed to structural inequities, and by patient sex.

The hyperthermic property of stimulants are well documented in animal and human studies, particularly for 3,4-Methylenedioxymethamphetamine (MDMA) and cocaine (Liechti 2014, Lomax and Daniel 1993, Parrott 2012). Stimulants can increase heat production by increasing metabolic activity, and impair heat dissipation by reducing peripheral blood flow

as well as the delayed the onset of diaphoresis (Freedman et al. 2005, Mills et al. 2004, Rusyniak and Sprague 2005). Synergistic effects between stimulant and ambient temperature to induce hyperthermia have also been observed in rats (Cassel et al. 2007, Dafter 1995, Kiyatkin et al. 2014). MDMA and cocaine both have a deleterious effect on centrally mediated thermoregulation through their effects on dopamine, norepinephrine, and serotonin (Docherty and Alsufyani 2021a, Docherty and Alsufyani 2021b).

In addition to their impacts on thermoregulation, amphetamine and cocaine use are associated with rhabdomyolysis, leading to acute renal injury (Halachanova et al. 2001, Mansoor et al. 2017). Complicating the rhabdomylosis and kidney injury is dehydration from decreased fluid intake (Isoardi et al. 2019, Young et al. 2020), which may be exacerbated by increased ambient temperatures (Sherbakov et al. 2018). Recent studies have also reported associations between stimulants and various adverse cardiovascular outcomes, including arrhythmia, heart failure, and myocardial infarction (Dominici et al. 2022, Tadrous et al. 2021). Multiple studies have found associations between higher ambient temperature and ED visits for kidney and cardiovascular outcomes in the general population (Chen et al. 2017, Kim et al. 2019, Knowlton et al. 2009, Sun et al. 2021), and the vulnerability to heat exposure may be enhanced among people who use stimulants.

The effects of opioids on thermoregulation are more complex and its ability to directly cause hyperthermia is unclear (Rawls et al. 2011). First, our observed opioid use/overdose ED visits association with higher temperature may be due to the sedating effects of opioids. For example, decreased alertness and drowsiness may impact the patient's ability to mitigate heat exposures. Second, opioid use disorder is also associated with various chronic health conditions that are sensitive to ambient heat (Scott et al. 2016, Wu et al. 2018).

The observed positive associations between temperature and substance use/overdose may also be partially explained by the patient's risk environment, behavior during warm temperature, impaired nutritional state, and physical health. Previous studies have reported higher rates of amphetamine and cocaine initiation during the summer due to increased idle time and willingness to use drug (Palamar et al. 2020). Furthermore, individuals who use drugs recreationally may not avoid higher ambient temperature as evidenced by the narrative of a heightened effect of ecstasy in dance clubs, raves, and festival settings due to higher ambient temperatures (Bedi and Redman 2006). These environments are particularly dangerous for heat-related illness due to crowding, limited access to water, and hot temperature (Palamar and Sonmez 2022). On the other hand, people who use drugs and are homeless have reported using methamphetamine to stay warm during nights. Further research, informed by people who use drugs, is needed to understand the role of multi-drug use patterns and the impact of the environment on drug use behavior and decision-making.

There are important implications for climate health equity planning if there are relationships between substance use behaviors and ambient temperature, in California and beyond. Both the California Department of Public Health (CDPH, 2023), and the United States federal government's Department of Health & Human Services have re-organized to support major efforts around climate change and health equity that acknowledge population vulnerabilities to climate change may be heterogeneous and reflect prior disparities. Impacts on substance

use behaviors should be considered as well. The social patterning of substance use is nuanced according to intersectional identities of race, gender, and sexual orientation, all of which are important dimensions for achieving health equity (Mereish et al. 2014, Vu et al. 2019). Taking an intersectional approach toward achieving population health equity, and in particular environmental justice and equitable climate resilience (Alvarez and Evens 2021, Ryder 2017, Malin and Ryder 2018, Versey 2021) may require holistically examining health disparities including aspects not commonly evaluated in environmental health research (e.g., substance use behaviors and the relationship between substance use and the environment).

This study has several strengths. First, temperature exposures were based on an observation-based data product with fine spatial resolution and complete spatial coverage, which may reduce exposure measurement error compared to only using monitoring data (Thomas et al. 2021). Second, the number of substance use ED visits in this study was large, allowing us to separately examine associations by substance type, and by use versus overdose. Third, we conducted extensive sensitivity analyses that include comparing different daily temperature metrics and different forms of the exposure–response functions.

The study also has limitations. First, substance use and overdose were ascertained using ICD codes on hospital billing records at the ED encounter, which is likely to under-ascertain cases compared to those ascertained from longitudinal medical records and or surveys of people who use drug. While daily temperature is likely to be independent of outcome misclassification due to diagnosis, temperature may impact the likelihood of an ED encounter. Second, we used the outdoor temperatures as a proxy for the person exposure, which is influenced by an individual's time-activity pattern. We expect this source of exposure measurement to be non-differential between case and control days within an individual, and may bias estimated associations towards the null. In our study, risks associated with daily maximum and daily average are slightly weaker compared to daily minimum (Fig. 2). This may suggest that minimum temperature may have less measurement error since it better corresponds to night-time temperature where individuals are at home. Finally, we did not examine effect modification by area-level covariates, including climatic regions, which may be associated with adaptation and resilience to extreme heat.

In conclusion, our study suggests that people who use stimulants and opioids may be a subpopulation sensitive to short-term higher ambient temperature. Several important research areas warrant future investigations to help identify harm reduction strategies. There is a need to better understand how people who use drug modify behaviors in response to high temperature and what are their health care utilization needs during heat stress. The built and social environments can influence drug use behaviors and experiences (Ezell et al. 2021); but how they interact with heat exposures is unclear as access to vacant homes and greenspace may be important for unhoused individuals. In addition, the role of polysubstance use should be further characterized given its increasing prevalence, unique risk profile and adverse consequences. A more detailed examination severity and symptom-related diagnosis and procedure codes (e.g., rhabdomyolysis, fluid depletion, heat stroke/exhaustion, and hyperthermia) among our ED visit cases may shed insights on the morbidity associated with increased environmental temperature. Finally, more research is needed to explore the nuanced social patterning of these relationships, which should also reflect input

from persons who use drugs, consider the intersectionality of place and membership in marginalized groups, to reduce the risk of further stigmatization, ensure interpretability of results, and facilitate meaningful translation of research.

5. Studies in humans and animals

The authors state that the study does not involve informed consent and only relies on secondary data analysis. The study was approved the Institutional Reviewer Board at Emory University for human subject research.

6. Data Statement

The authors are unable to share the emergency department visit data due to the Data Use Agreement regarding protected health information. Interested individuals can directly request similar data from the California Office of Statewide Health Planning and Development.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data availability

The authors do not have permission to share data.

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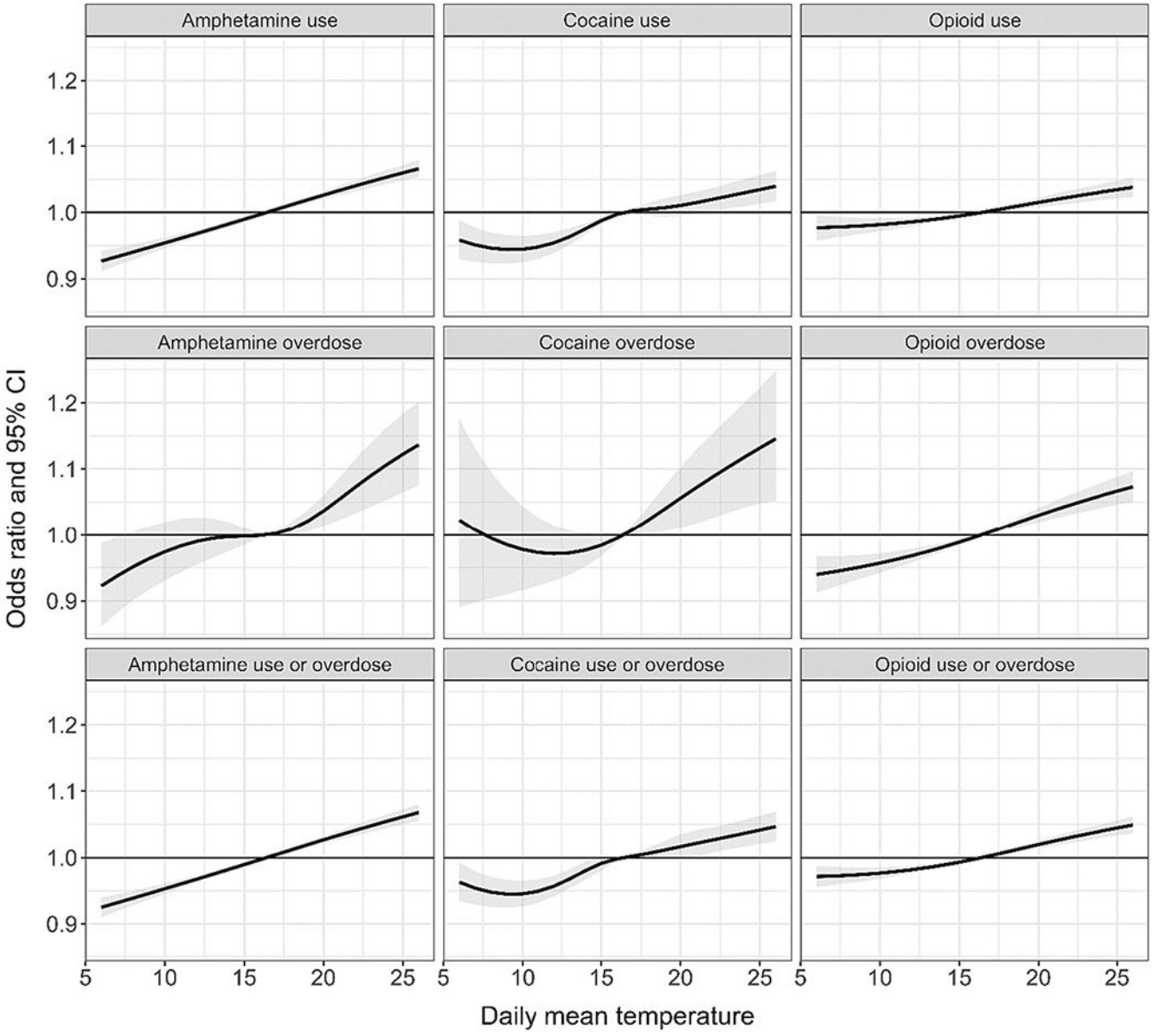

Fig. 1.

Exposure-response curve for associations between substance use and overdose emergency department visits and 4-day cumulative daily mean temperature (°C) in California, 2005–2019. Reference exposure level is defined as the median of daily mean temperature (16.41 °C). 95% confidence intervals (CIs) are shown by ribbons around the curves.

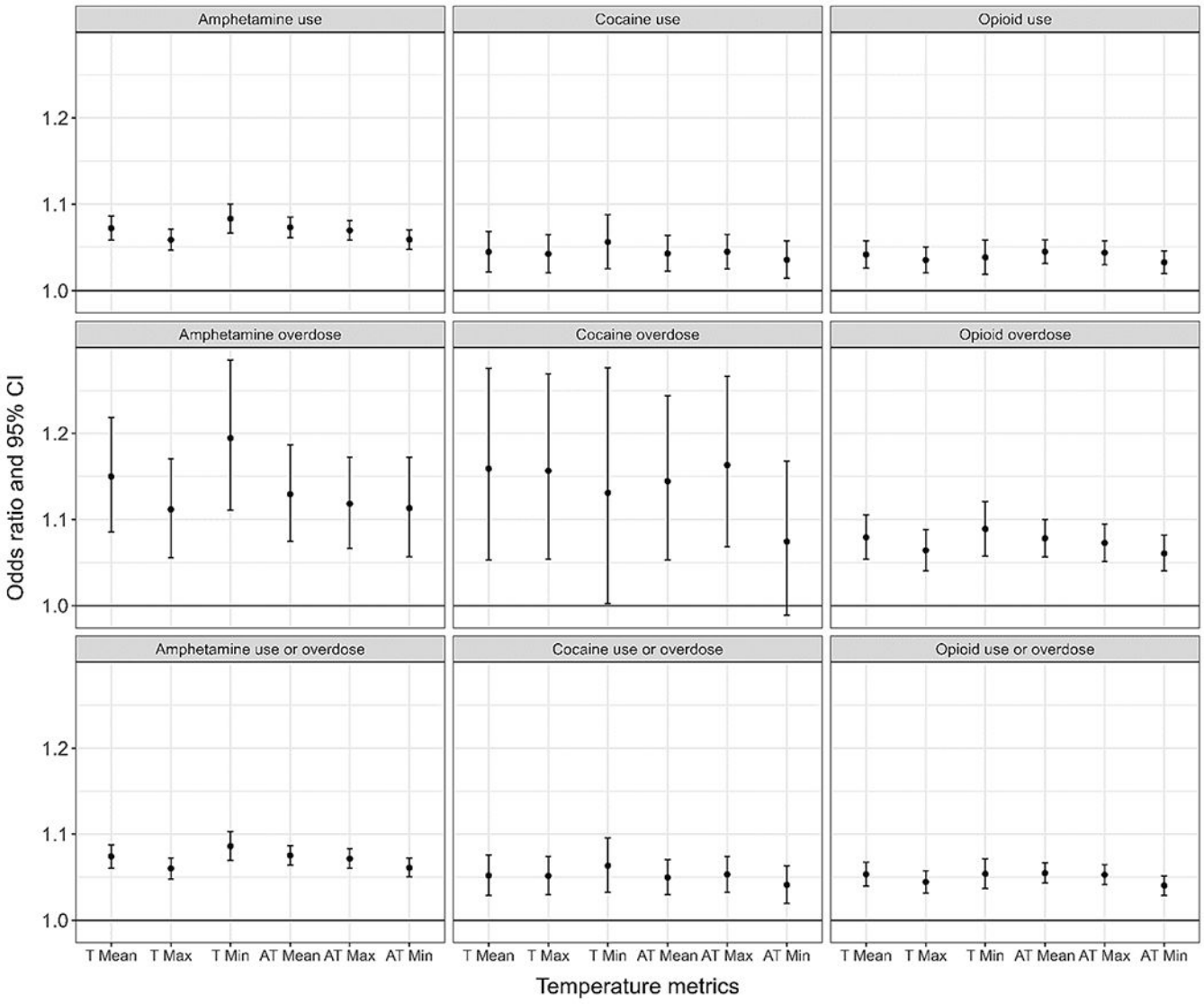

Fig. 2.

Odds ratios (ORs) of substance use/overdose emergency department visits comparing the 95th percentile to the 50th percentile of different temperature metrics (4-day cumulative exposures). T Mean: daily mean temperature; T Max: daily maximum temperature; T Min: daily minimum temperature; AT Mean: daily mean apparent temperature; AT Max: daily maximum apparent temperature; AT Min: daily minimum apparent temperature.

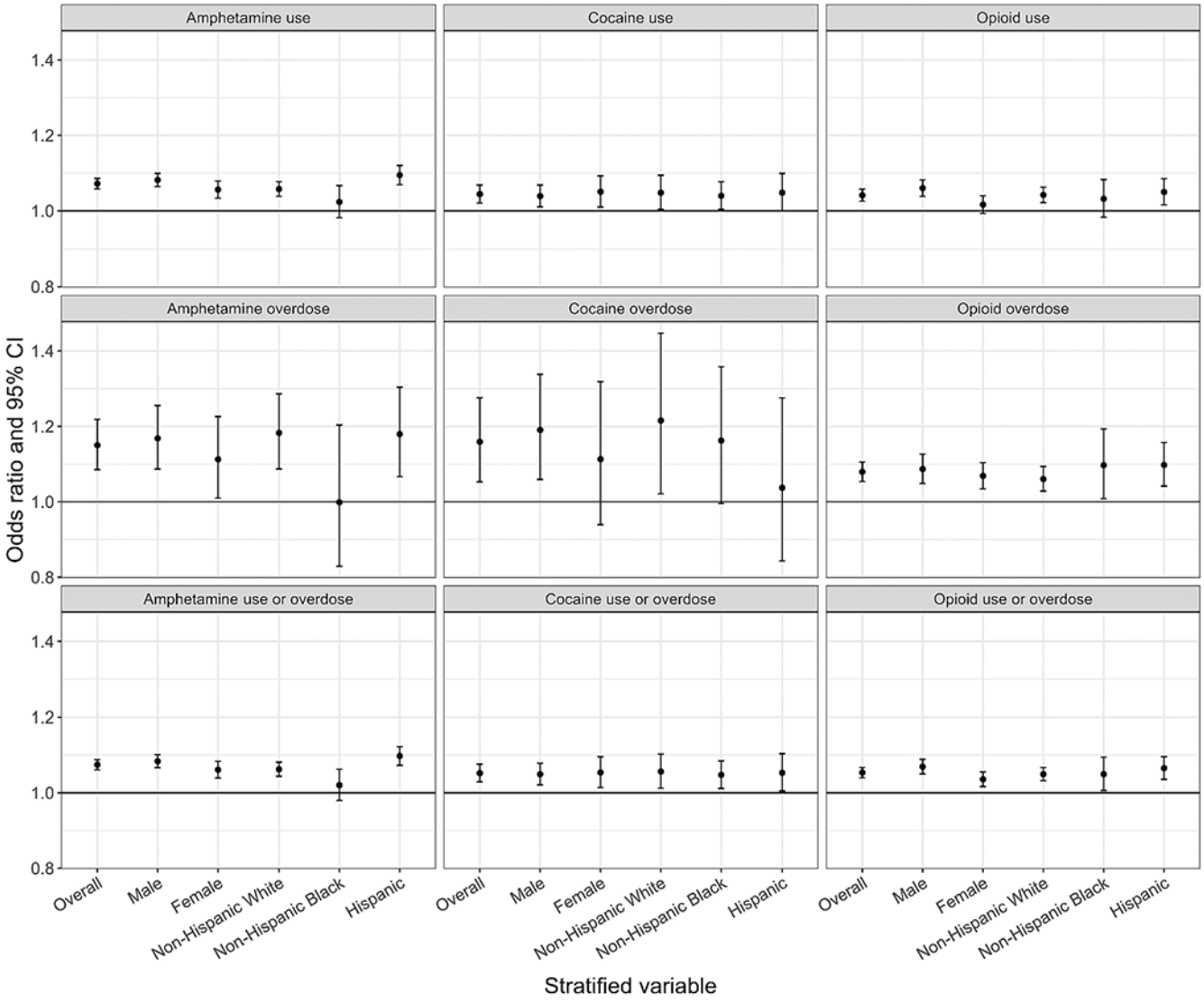

Fig. 3.

Odds ratios and 95% confidence intervals associated with substance use/overdose emergency department visits comparing the 95th percentile and 50th percentile of daily mean temperature stratified by effect modifiers: race/ethnicity (Hispanic, Non-Hispanic White, Non-Hispanic Black) and sex (Male, Female). The overall estimates denote non-stratified results.

Table 1

Number of substance use or overdose emergency department visits for amphetamine, cocaine and opioid, stratified by demographics in California during 2005–2019.

Demographics	Amphetamine	Amphetamine overdose	Cocaine	Cocaine overdose	Opioid use	Opioid overdose
	(N = 1,496,401)	(N = 77,761)	(N = 518,256)	(N = 24,201)	(N = 890,265)	(N = 403,547)
Sex						
Female	532,760	27,466	173,716	7,843	403,983	222,041
Male	963,383	50,248	344,347	16,321	486,146	181,429
NA	258	47	193	37	136	77
Age group						
0–17	28,207	8,343	6,980	669	5,918	12,768
18–29	384,541	22,436	103,611	6,140	165,456	62,130
30–44	550,947	23,917	142,279	6,515	233,440	73,085
45–64	497,857	21,091	239,831	9,685	380,572	136,846
65+	34,849	1,974	25,555	1,192	104,879	118,718
Race/Ethnicity						
Hispanic	457,232	24,093	113,741	4,977	184,526	81,383
Non-Hispanic White	754,599	37,733	143,953	7,215	549,118	250,372
Non-Hispanic Black	155,572	7,799	224,708	10,035	101,772	35,067
Non-Hispanic Asian/Islander	34,310	2,633	9,392	568	11,381	14,144
Others	53,152	2,909	12,728	650	25,943	12,873
NA	41,536	2,594	13,734	756	17,525	9,708