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# The effect modification of extreme temperatures on mental and behavior disorders by environmental factors and individual-level characteristics in Canada

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# ABSTRACT

Objective: Ambient extreme temperatures have been associated with mental and behavior disorders (MBDs). However, few studies have assesed whether vulnerability factors such as ambient air pollution, pre-existing mental health conditions and residential environmental factors increase susceptibility. This study aims to evaluate the associations between short-term variations in outdoor ambient extreme temperatures and MBD-related emergency department (ED) visits and how these associations are modified by vulnerability factors. *Methods:* We conducted a case-crossover study of 9,958,759 MBD ED visits in Alberta and Ontario, Canada made between March 1st, 2004 and December 31st, 2020. Daily average temperature was assigned to individual cases with ED visits for MBD using gridded data at a 1 km  $\times$  1 km spatial resolution. Conditional logistic regression was used to estimate associations between extreme temperatures (i.e., risk of ED visit at the 2.5th percentile temperature for cold and 97.5th percentile temperature for heat for each health region compared to the minimal temperature risk) and MBD ED visits. Age, sex, pre-existing mental health conditions, ambient air pollution (i.e.  $PM_{2.5}$ ,  $NO_2$  and  $O_3$ ) and residential environmental factors (neighborhood deprivation, residential green space exposure and urbanization) were evaluated as potential effect modifiers.

Results: Cumulative exposure to extreme heat over 0–5 days (odds ratio [OR] = 1.145; 95% CI: 1.121–1.171) was associated with ED visits for any MBD. However, cumulative exposure to extreme cold was associated with lower risk of ED visits for any MBD (OR = 0.981; 95% CI: 0.976–0.987). We also found heat to be associated with ED visits for specific MBDs such as substance use disorders, dementia, neurotic disorders, schizophrenia and personality behavior disorder. Individuals with pre-existing mental health conditions, those exposed to higher daily concentrations of  $NO_2$  and  $O_3$  and those residing in neighborhoods with greater material and social deprivation were at higher risk of heat-related MBD ED visits. Increasing tree canopy coverage appeared to mitigate risks of the effect of heat on MBD ED visits.

 ${\it Conclusions}$ : Findings provide evidence that the impacts of heat on MBD ED visits may vary across different vulnerability factors.

# 1. Introduction

Climate change is a significant public health concern globally. It

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adversely affects health by influencing weather, ecosystems and human systems (Ebi et al., 2021a; Romanello et al., 2021). Extreme heat events

### **Abbreviations**

AIC Akaike Information Criterion
BLUP best linear unbiased predictions
DLNM distributed lag non-linear models
ED emergency department

ED emergency department LICO low-income cutoff

MBD mental and behavior disorder

MSDI Material and Social Deprivation Index NDVI normalized difference vegetation index

OEDT optimal ED visit temperature

OR odds ratio

95%CI 95% confidence interval

are likely to become more frequent and intense, bringing prolonged periods of extreme high temperatures (i.e., heat) compared to regional averages (Ebi et al., 2021b). Ambient extreme temperatures have been found to be significantly associated with total and cause-specific morbidities (Ye et al., 2012; Xu et al., 2020). A growing number of studies have also reported associations between extreme temperatures and the psychotic exacerbation of core symptoms for many mental and behavior disorders (MBDs). In fact, several studies have demonstrated increases in self-reported adverse mental health outcomes, including emergency department (ED) visits and hospital admissions, during periods of extreme temperatures (Bundo et al., 2021; Carlsen et al., 2019; Mullins and White, 2019; Niu et al., 2020; Nori-Sarma et al., 2022; Qiu et al., 2022; Yoo et al., 2021a, 2021b; Wang et al., 2014).

The adverse effects associated with extreme temperatures do not affect people and communities equally. Individual sociodemographic factors, including age, sex, and socio-economic status, may modify the effect of heat on health (Romanello et al., 2021; Ho et al., 2018). Additionally, environmental and contextual factors, such as the level of urbanization, access to green space and neighborhood deprivation, have been found to modify the relationship between heat and health (Ye et al., 2012; Henderson et al., 2022; Jay et al., 2021; Son et al., 2022; Heo et al., 2021; Sera et al., 2019a). However, there is limited evidence regarding whether specific individual-level factors such as age, sex and pre-existing mental health conditions increase susceptibility to MBDs when individuals are exposed to extreme ambient temperatures. In addition, little evidence exists on whether specific environmental factors can amplify (e.g. higher levels of ambient air pollution, level of deprivation, urbanization) or attenuate (e.g. access to green space) the effects of extreme temperatures on MBDs (Hwong et al., 2022). In fact, very few evidence exists on whether associations between extreme ambient temperatures and MBDs can be modfied by levels of ambient air pollution (Qiu et al., 2022). Moreover, fewer studies have assessed the impact of extreme low temperatures (i.e., cold) on MBDs.

The general objective of this study was to test the hypothesis that short-term variations in extreme temperatures increase the risk of ED visits for MBDs. We also hypothesized that the association between short-term variations in temperatures and MBD ED visits is modified by vulnerability factors related to individual-level and residential environmental factors.

# 2. Methods

# 2.1. Study design

We conducted a case-crossover study across 40 health regions in the

provinces of Alberta and Ontario in Canada where associations between daily fluctuations in ambient temperatures and MBD ED visits were evaluated. In a case-crossover study, cases are their own control, which is an appropriate study design for short term exposures (Maclure, 1991). Specifically, the exposure on the day of admission to the ED for MBD is compared to control periods, which are identified through a time-stratified approach (Janes et al., 2005; Bateson and Schwartz, 2001; Jaakkola, 2003; Navidi and Weinhandl, 2002). These control periods are identified using the same day of the week on which the ED visit for MBD occurred, but using those other days during the same month and year as the ED visit. The ends up capturing 3 or 4 referrent control periods. For instance, if an ED visit for MBD occurred on the first Monday of January 2020, the control periods would be identified during those other Mondays during the month of January 2020. Therefore, this approach of matching the case and control periods adjusts for any influence from the day-of-the-week and month. This study design is also less prone to bias from time trends since it accounts for any seasonal effect and also accounts for individual-level confounders (e.g. smoking status) that are not expected to vary on a short term basis (Janes et al., 2005; Levy et al., 2001; Schwartz, 2004). Ethics approval for this study was granted through a data sharing agreement between Health Canada and the Canadian Institute for Health Information (CIHI).

# 2.2. Health outcomes and data

We extracted all ED admissions for MBD from the National Ambulatory Care Reporting System (NACRS) database administered by CIHI that occurred between March 1st, 2004 and December 31st, 2020 in 5 health regions in the province of Alberta and 35 health regions in the province of Ontario (Gibson et al., 2008). We included ED visits regardless if these resulted or not in subsequent hospital admission. We did not have data for the other Canadian provinces due to underreporting of ED visits (i.e. not all hospitals are reporting the ED data) to the NACRS database and that only Alberta and Ontario had mandated reporting. The universal health care coverage in Canada ensures that the NACRS database contains all ED admissions in those two provinces. We used the International Classification of Diseases [ICD]-10th revision codes in order to capture specific diagnoses of MBDs (Bundo et al., 2021; Nori-Sarma et al., 2022; Yoo et al., 2021b; Wang et al., 2014): any MBD (F00-F99), psychoactive substance use (F10-F19), schizophrenia (F20-F29), mood disorder (F30-F39), neurotic disorder (F40-F59), personality behavior disorder (F60-F69), developmental disorder (F80-F98) and dementia (F00-F03). We also extracted information on the following pre-existing mental health conditions in order to evaluate whether those conditions increase susceptibility for MBD ED visits during periods of extreme temperatures: schizophrenia, mood disorder, neurotic disorder, personality behavior disorder, developmental disorder and dementia. We used a determinitic linkage using encrypted health card numbers in order to link the NACRS database with the Discharge Abstract Database (DAD), a database capturing hospital admissions (Lavigne et al., 2014). One hospitalization or ED visit in the year prior to the index MBD ED visit in either the DAD or NACRS for the medical condition under consideration was considered for identifying a pre-existing condition. Demographic informations were extracted from the NACRS database which included age, sex, and postal code of residence. We excluded cases with missing information on postal code, those that resided outside of Alberta and Ontario in order to reduce exposure measurement error and readmissions within 30 days following the index event were excluded (i.e., if the same person was re-admitted to an ED within 30 days, only the first visit was included).

# 2.3. Weather data

We extracted data on daily average ambient temperature and water vapour pressure from the Daymet dataset at a 1 km  $\times$  1 km grid spatial resolution across Canada (Thornton et al., 2021). The mean daily

relative humidity was derived from the Bolton equation (Williams and Ambaum, 2021). Statistics Canada's population ecumene boundary was used to retrieve the weather parameters only above inhabited land (Statistics Canada, 2017). Case and control periods (described below) with postal codes within each grid of the surfaces were assigned exposures accordingly. The final result is the mean of all the grid cells within each postal code.

# 2.4. Environmental and contextual factors

Health-region level information were captured in order to reduce and explain levels of heteregoneity that may exist across health regions. These were subsequently used in a meta-regression model (explained below). These factors, derived from census data, included information on population density, percent of the population in the health region with income less than the low-income cutoff (LICO) in Canada, percent of the population in the health region self-identified as Black and percent of the population in the health region living in an urban area (Stieb et al., 2020). We also captured information on the percent of the population in the health region who rate their health as fair or poor, derived from 2018 Canadian Community Health Survey (CCHS) (Statistics Canada, 2021). Finally, we derived variables classifying the health region's climate using the long term mean temperature and temperature range (Cakmak et al., 2018).

Cases' 6-character postal codes were used to link potential residential environmental effect modifiers (neighborhood deprivation, residential green space exposure, and urbanization). The data was obtained from the Canadian Urban Environmental Health Research Consortium (CANUE) (Brook et al., 2018). The neighborhood deprivation was characterized using the Material and Social Deprivation Index (MSDI) derived from Canadian census data (Pampalon et al., 2012; CanMap Postal Code Suite v2015, 2015). Three indicators describe the material component of this index which are the proportion of people aged 15 or older without a secondary school diploma (or equivalent), the proportion of people who are emplyed aged 15 or older and the average income of people aged 15 or older. Three indicators also characterize the social component: the proportion of people aged 15 or older living alone, the proportion of people aged 15 or older separated, divorced or widowed, and the proportion of single-parent families. The neighborhood quintiles for each province from 2006, 2011 and 2016 censuses were obtained and were converted into five deprivation categories using (Gamache et al., 2019): (1) materially and socially privileged; (2) average material and social deprivation; (3) materially privileged but socially deprived; (4) materially deprived but socially privileged and (5) materially and socially deprived. The neighborhood deprivation category from the closest census year was linked to the MBD ED visit.

We extracted hourly ambient air pollution concentrations using fixed-site monitors located in each of the 40 health regions and managed by the National Air Pollution Surveillance Program of Environment and Climate Change Canada (ECCC). (Environment Canada, 2022). Hourly concentrations of fine particulate matter less than 2.5  $\mu m$  (PM $_{2.5}$ ), nitrogen dioxyde (NO $_{2}$ ) and ozone (O $_{3}$ ) were averaged to create daily averages and we averaged all daily values across all monitoring stations for each health region. We then assigned ambient concentrations of air pollution by residential postal code for case and control periods.

The other residential environmental factors, residential green space and urbanization, were assessed by extracting their levels using buffers from centroid coordinates of residential postal codes.

The normalized difference vegetation index (NDVI) using the maximal annual value of the growing season was extracted from Landsat (30 m  $\times$  30 m) (Spatial Inc, 2015; Gorelick et al., 2017; USGS Landsat 5 TM TOA, 1984; USGS Landsat 8 TOA Reflectance, 2013) in order the characterize exposure greenness in the residential environment. Barren surfaces are usually characterized by NDVI values less than 0.2, grasslands by values from 0.2 to 0.4 and values greater than 0.4 indicate increasingly lush vegetation (Robinson et al., 2017). Long term tree

canopy coverage was also obtained as a measure of exposure to greenness (Gorelick et al., 2017; DMTI Spatial Inc, 2010; Sexton et al., 2013). Tree canopy is defined as area of vegetation (including leaves, stems, branches, etc.) of woody plants estimated by the percent of pixels covered by vegetation greater than 5 m in height. Both greenness metrics were available for buffer areas ranging from 100 to 1000 m, but we used a buffer of 100 m for tree canopy coverage and 250 m for NDVI, based on preliminary analyses. Finally, we extracted the percent of area characterized as urban, based on CANUE's Local Climate Zone data (Spatial Inc, 2015; Bechtel et al., 2015). We categeorized the environmental factors in tertiles in order to evaluate their modifying effects.

# 2.5. Statistical analysis

The statistical analyses were conducted in two stages. We first used conditional logistic regressions separately for each health region in order to assess the associations between daily flucturations in ambient temperatures ED visits for MBDs. Then, we pooled the overall estimate using multivariate meta-regression models. We used the R software (version 4.1.1)<sup>50</sup> with packages *survival*, *dlnm* and *mixmeta*.

# 2.6. First stage modeling

Odds ratios (ORs) and their 95% confidence intervals (CIs) were obtained by fitting conditional logistic regression models in order to apply the case-crossover analysis (Maclure, 1991). Models were first fitted by considering a lag period of up to 5 days (i.e. lag 0 to lag 5) before the ED visit or the control period consideing single lag day effects and cumulative effects (i.e. effects over 0-5 days). All lag periods were described with distributed lag non-linear models (DLNMs) in order to account for both the temperature-ED visit relationship as well as the potential delayed/lagged response (Gasparrini, 2014). The lag period selection was based on prior literature evaluating daily fluctuations in ambient temperatures on MBD ED visits (Nori-Sarma et al., 2022; Yoo et al., 2021b) and by conducting preliminary analysis (see supplementary material, Figure S1). We combined our conditional logistic regression models with DLNMs (Gasparrini, 2014). Temperature-ED visit non-linear exposure-response association was accounted for using quadratic B-splines with three internal knots placed at the 10th, 75th and 90th percentiles of each health region's specific temperature distributions. We also accounted for the non-linearity in daily relative humidity exposure-response function using natural cubic splines with three degrees of freedom (Gasparrini et al., 2015). The different decisions for knot selections and degrees of freedom were based on Akaike Information Criteria (AIC) as well as visual inspections of preliminary findings.

# 2.7. Second stage modeling

The ORs for each health region evaluating impacts of ambient temperatures on MBD ED visits were pooled into a multivariate metaregression (Sera et al., 2019b). The pooling of the effect allowed to derive and improve estimates of temperature-MBD ED visit associations by using best linear unbiased predictions (BLUP). Information across the health region level are borrowed in order to improve estimates. The meta-analysis was repeated for each sub-categories of MBDs. In this study, we reported the ORs of ED visits for MBDs relative to the reference temperature, hereafter referred to as optimal ED visit temperature (OEDT). The OEDT was obtained by identifying the temperature related to minimal risk of MBD ED visit by scanning across the 5th and 95th percentile of the temperature distribution in each health region (Yoo et al., 2021b). This approach has been previously used to identify the OEDT ensuring that extreme values would be excluded from the minimal temperature risk (Yoo et al., 2021b). The effect of heat was calculated as the risk of ED visit at the 97.5th percentile temperature for each health region and the effect of cold as the effect at the 2.5th percentile

temperature for each health region. Meta-regression models were fitted with and without health-region level information in order to evaluate whether these factors explained heterogeneity of temperature-MBD associations. Multivariate Wald test were used to evaluate the significance of health region level factors along with and Cochran's Q-test and  $\rm I^2$  statistic.

# 2.8. Subgroup analysis

We conducted stratified analyses within the first- and second-stage modeling domains described above in order to obtain ORs by predefined categories of age (<18, 18-29, 30-49 & > 50), sex, neighborhood deprivation, air pollution, tree canopy, NDVI, urbanicity area and pre-existing mental health conditions. We divided the air pollutants into three levels: low (≤ health region-specific 10th percentile value), medium (between the health region-specific 10th and 90th percentile values) and high (≥ health region-specific 90th percentile value). Effect modification by those characteristics were evaluated in temperature-ED visit associations. The statistical significance was tested using a multilevel meta-regression model using the individual-level characteristics multivariate outcomes sharing the same health region random effect. We subsequently applied a Wald test to evaluate the significance of effect modification (Sera et al., 2019b). We evaluated the effect modification when considering each modifier as a categorical variable using a common reference category (Xu et al., 2021) and assessed the potential modifer as a continuous predictor in order to evaluate whether a trend exists in the effect modification.

# 3. Results

In total, there were 9,958,759 ED visits for MBDs in Alberta and Ontario between March 1st, 2004 and December 31st, 2020. Most cases were observed in Ontario, were 30–49 years of age (33.8%) and were females (53.2%). Characteristics of the study population are shown in Table 1. Table 2 shows the descriptive statistics for weather and environmental variables. The average daily mean temperature was 5.95 °C, varying from –34.85 to 31.61 °C (interquartile range of 16.26 °C). The average tree canopy coverage within 100 m of the centroid of postal codes was 19.6% and the average NDVI within 250 m of the centroid was 0.36. In Supplementary Table S1, we found weak correlations between ambient air pollutant variables and tree canopy coverage and NDVI.

Table 3 shows the associations between daily average temperature

Table 1
Number of emergency department visits for mental and behavior disorders across 40 health regions in Alberta and Ontario, Canada between March 1st 2004 and December 31st 2020 by specific characteristics.

Variable	Number of ED visits (%)		
Age (in years)			
<18	1,430,690 (14.7)		
18–29	2,466,071 (24.8)		
30-49	3,368,557 (33.8)		
≥50	2,693,674 (27.1)		
Sex			
Male	4,659,061 (46.8)		
Female	5,298,976 (53.2)		
Combined material and social deprivation index			
Materially and socially privileged	1,831,645 (18.4)		
Average material and social deprivation	2,312,281 (23.2)		
Materially privileged but socially deprived	1,950,637 (19.6)		
Materially deprived but socially privileged	2,046,954 (20.6)		
Materially and socially deprived	1,817,475 (18.3)		
Province			
Alberta	3,775,811 (37.9)		
Ontario	6,182,948 (62.1)		
Total ED visits	9,958,759 (100.0)		

ED, emergency department.

**Table 2**Descriptive statistics of environmental variables.

Variable	Mean (SD)	Median	IQR	Range
Temperature (° C)	5.95 (10.91)	6.81	16.26	-34.85-31.61
Relative humidity (%)	62.42 (16.90)	65.31	20.17	12.11-99.32
$PM_{2.5} (\mu g/m^3)$	10.00 (6.71)	8.47	6.55	0.06-141.60
NO <sub>2</sub> (ppb)	13.86 (7.80)	12.08	10.40	0.25-63.68
O <sub>3</sub> (ppb)	40.63	12.31	17.00	1.01-107.10
Tree canopy within 100 m (%)	19.57 (8.22)	19.50	11.52	1.50-41.03
NDVI within 250 m	0.36 (0.08)	0.35	0.10	0.02 - 0.68
Percent of urban area (%)	0.41 (2.15)	0.04	0.22	0.0-37.16

SD, standard deviation; IQR, interquartile range.

**Table 3**Odds ratios (ORs)<sup>a</sup> and 95% CIs for the associations between the cumulative effects of daily average temperature over 0–5 days and mental and behavior-related emergency department visits in 40 health regions across Alberta and Ontario, Canada (2004–2020).

Diagnosis	Heat <sup>b</sup>	Cold <sup>c</sup>	I <sup>2</sup> (p-value for heterogeneity) <sup>4</sup>
Any mental health condition	1.145 (1.121–1.171)	0.981 (0.976–0.987)	$I^2 = 61.7\% \ (<0.01)$
Substance use disorders	1.289 (1.244–1.334)	0.972 (0.963–0.981)	$I^2 = 68.8\% \ (<0.01)$
Schizophrenia	1.152 (1.104–1.202)	0.981 (0.972-0.989)	$I^2 = 34.3\% \ (<0.01)$
Mood disorders	0.995 (0.973–1.016)	0.985 (0.959–1.011)	$I^2 = 56.8\% \ (<0.01)$
Neurotic disorders	1.153 (1.120–1.186)	0.979 (0.972–0.986)	$I^2 = 51.7\% \ (<0.01)$
Personality behavior disorder	1.109 (1.042–1.181)	0.971 (0.942–1.000)	$I^2 = 42.1\% \ (<0.01)$
Developmental disorder	0.992 (0.978–1.006)	1.013 (0.919–1.118)	$I^2 = 42.5\% \ (<0.01)$
Dementia	1.157 (1.067–1.255)	0.984 (0.956–1.014)	$I^2 = 0.0\% (0.58)$

 $I^2$ : The variance due to heterogeneity estimated by the  $I^2$ -statistic for the pooled models. In parentheses, the p-values for the statistical significance of heterogeneity are reported.

and ED visits for MBDs. Statistically significant associations were observed between the cumulative effect of heat over 0–5 days and ED visits for overall MBDs (OR = 1.145; 95% CI: 1.121–1.171). We also found heat to be associated with ED visits for specific MBDs, with the strongest effects observed for substance use disorders (OR = 1.289; 95% CI: 1.244–1.334) followed by dementia (OR = 1.157; 95% CI: 1.067–1.255), neurotic disorders (OR = 1.153; 95% CI: 1.120–1.186), schizophrenia (OR = 1.152; 95% CI: 1.104–1.202) and personality behavior disorder (OR = 1.109; 95% CI: 1.042–1.181). The pooled cumulative exposure-response curves on ED visits for overall MBDs and subcategories of MBDs support the impact of heat on MBD ED visits and the lower risk associated with extreme cold temperatures (Fig. 1). We also found that accounting for population density, location-specific mean temperature and temperature range as meta-predictors in the

<sup>&</sup>lt;sup>a</sup> Models adjusted for daily mean relative humidity and health region-specific mean temperature and temperature range as meta-predictors. Models represent pooled health region-specific estimates derived using two-stage random effects meta-analysis and meta-regression incorporating population density, locationspecific mean temperature and temperature range as meta-predictors.

<sup>&</sup>lt;sup>b</sup> Defined as the 97.5th temperature percentile for each health region compared to the percentile of optimal ED visit temperature, where the minimum risk was identified between the 5th and 95th percentiles of temperature at the health region level.

<sup>&</sup>lt;sup>c</sup> Defined as the 2.5th temperature percentile for each health region compared to the percentile of optimal ED visit temperature, where the minimum risk was identified between the 5th and 95th percentiles of temperature at the health region level.

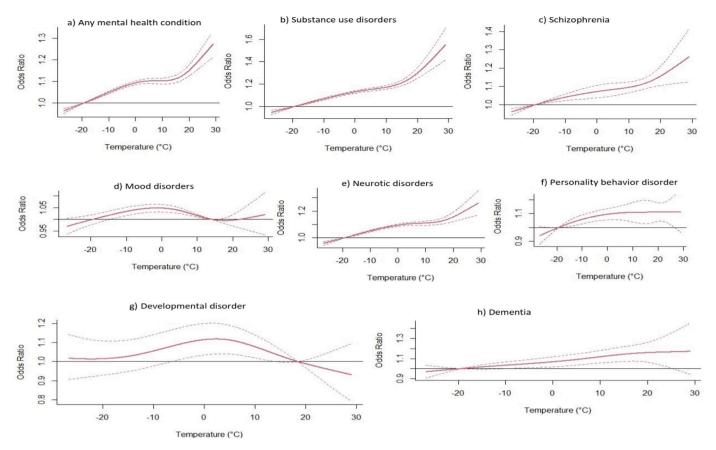


Fig. 1. Odds ratios (ORs) (Ebi et al., 2021a) and 95% CIs for the exposure-response associations between the cumulative effects of daily average temperature over 0–5 days and mental and behavior-related emergency department visits in 40 health regions across Alberta and Ontario, Canada (2004–2020).

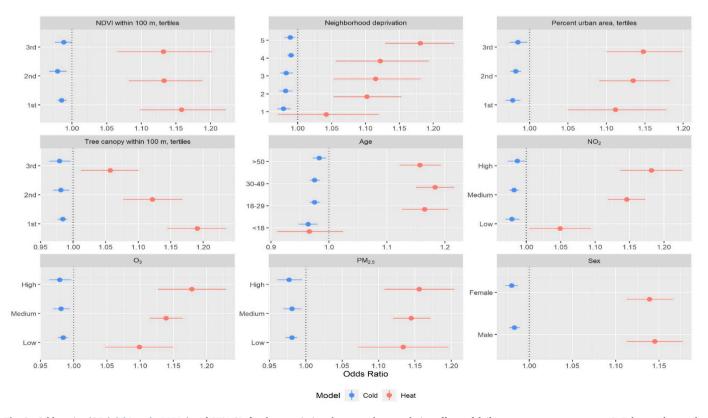


Fig. 2. Odds ratios (ORs) (Ebi et al., 2021a) and 95% CIs for the associations between the cumulative effects of daily average temperature over 0–5 days and mental and behavior-related emergency department visits in 40 health regions across Alberta and Ontario (2004–2020) stratified by selected characteristics.

meta-regression models further reduced the between-location heterogeneity, but the between-health region heterogeneity remained statistically significant, except for dementia.

The results of the stratified analyses examining the relationship between the cumulative effects of temperature over 0-5 days and MBD ED visits across individual-level and environmental and contextual characteristics are shown in Fig. 2 and Supplementary Table S2. When stratifying analyses by age, we found that the effect of heat on ED visits for any MBDs was highest among those aged 30-49 years (OR = 1.183; 95% CI: 1.150-1.216) and lowest among those aged less than 18 years (OR = 0.966; 95% CI: 0.911-1.024) (p-value for effect modification <0.01). We also found slightly higher effect estimates for the impact of heat on MBD ED visits among males (OR = 1.145; 95% CI: 1.113–1.177) compared to females (OR = 1.139; 95% CI: 1.113–1.166). There was a trend suggesting that impacts of heat are at their lowest among those who resided in materially and socially privileged neighborhoods (OR = 1.042; 95% CI: 0.971-1.119) and highest among those who lived in materially and socially deprived neighborhoods (OR = 1.181; 95% CI: 1.129-1.231) (p-value for trend = 0.02). Greenness exposure in the residential environment also appeared to attenuate impacts of heat on MBD ED visits, specifically increasing tree canopy coverage (p-value for trend = 0.01) while the evidence for NDVI and percent of urban area was not as clear. Finally, we found that the effect of heat on MBDs increased in a linear manner across categories of NO2 and O3 (p-values for trend ≤0.04). For instance, we found that effect estimates for the impact of heat on MBDs were highest when exposure to  $NO_2$  (OR = 1.182; 95% CI: 1.137-1.227) and  $O_3$  (OR = 1.178; 95% CI: 1.127-1.229) were also highest. We did not find any evidence of effect modification by levels of PM<sub>2.5</sub>, although there was an increasing trend of the effect estimates through increasing categories of PM<sub>2.5</sub>.

Stratum-specific estimates by pre-existing mental health condition showed that those with prior diagnosis of mood disorders, neurotic disorders, personality behavior disorders and developmental disorders had an increased risk for impacts of heat compared to those without those conditions (p-values for effect modification  $\leq$ 0.05) (Fig. 3 and

Supplementary Table S3). There were also no clear patterns observed for exposures to cold temperatures. In sensitivity analyses, we found that the temperature effects on MBD ED visits were similar when using different maximum lag days, different values for the degrees of freedom for temperature and humidity and additional adjustment for ambient air pollutants (Supplementary Table S4).

### 4. Discussion

Using individual-level data, this study showed that exposure to extreme heat was associated with overall MBD ED visits and ED visits for subcategories of MBDs. We also found that the associations between extreme heat and MBD ED visits were stronger among those aged 30–49 years and among those with the highest level of neighborhood deprivation. Residential exposure to increasing tree canopy coverage appeared to play a beneficial role in mitigating the effect of exposure to extreme heat while higher daily levels of NO<sub>2</sub> and O<sub>3</sub> appeared to enhance the risk of heat on MBD ED visits. Individuals with pre-existing MBDs appeared to be at highest risk of exposure to heat and the exacerbation of MBDs.

We found that exposure to extreme heat, but not extreme cold, was associated with increased risk of ED visits for overall MBDs and subcategories of MBDs. The fact that we did not observe increased risk for MBD ED visits during extreme cold temperatures is consistent with previous evidence (Yoo et al., 2021b; Wang et al., 2014; Hansen et al., 2008; Zhang et al., 2020; Lee et al., 2018). Previous studies have also found associations between exposure to extreme heat and ED visits for MBDs (Bundo et al., 2021; Carlsen et al., 2019; Mullins and White, 2019; Niu et al., 2020; Nori-Sarma et al., 2022; Qiu et al., 2022; Yoo et al., 2021b; Wang et al., 2014), although the evidence for the impact on subcategories of MBDs remains to be clarified. In particular, our findings for the impact of extreme heat on specific subcategories of MBDs corroborate previous studies that have also found impacts on substance use disorders (Niu et al., 2020; Nori-Sarma et al., 2022; Yoo et al., 2021b; Wang et al., 2014), schizophrenia (Nori-Sarma et al., 2022;

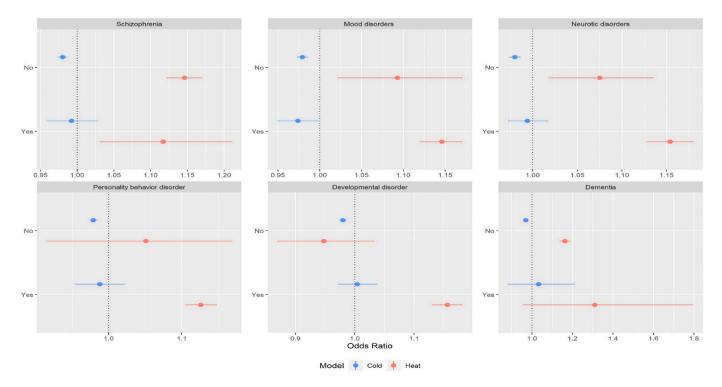


Fig. 3. Odds ratios (ORs) (Ebi et al., 2021a) and 95% CIs for the associations between the cumulative effects of daily average temperature over 0–5 days and mental and behavior-related emergency department visits in 40 health regions across Alberta and Ontario, Canada (2004–2020) stratified by selected comorbid mental health and behavioral conditions.

Oiu et al., 2022; Yoo et al., 2021b; Wang et al., 2014; Zhang et al., 2020; Yi et al., 2019), and neurotic disorders (Nori-Sarma et al., 2022; Qiu et al., 2022; Wang et al., 2014; Zhang et al., 2020). We also found a positive impact of extreme heat on ED visits for personality behavior disorders for which associations had been non-statistically significant in previous studies (Bundo et al., 2021; Nori-Sarma et al., 2022). Our findings also agree with the evidence of exacerbation of dementia during periods of high temperatures (Hansen et al., 2008; Lee et al., 2018; Linares et al., 2017; Ma et al., 2020; Wei et al., 2019). One thing to note is the heterogeneity in the magnitude of effects found in this study in the associations between extreme heat and specific subcategories of MBDs. For instance, substance use disorders had the highest OR. This could highlight the fact that extreme heat can induce psychological distress in those with mental health conditions which can lead to alcohol and substance abuse (Cianconi et al., 2020). Cognitive impairment could also be responsible for impacts on outcomes such as schizophrenia, neurotic disorders and dementia making these individuals more susceptible to environmental factors (Cianconi et al., 2020).

In terms of the age group that was most susceptible to exacerbations to heat on MBD ED visits, we found that those aged 30 to 49 were at the highest risk, which corroborates previous evidence that also found middle-aged adults to be at higher risk (Nori-Sarma et al., 2022; Yoo et al., 2021a), although heterogeneity of effect across age groups is still not clear (Nori-Sarma et al., 2022). Similar to previous studies, we did not find significant effect modification by sex (Bundo et al., 2021; Nori-Sarma et al., 2022; Yoo et al., 2021b).

The evaluation of residential environmental factors represents an important avenue in identifying those most vulnerable to the impact of extreme heat on MBD ED visits. For instance, we found that increasing neighborhood deprivation was associated with higher risk of MBD ED visits. Those living in areas that were more urbanized were also at higher risk. We also found that a higher exposure to greenness in the residential environment, in particular tree canopy, mitigated the impact of heat on MBD ED visits to some extent. Although this requires further research, increasing tree coverage may represent an important urban planning measure to reduce the burden of the impact of heat on mental health outcomes. There may be multiple explanations for this emerging finding. One is that trees may indeed act as a modifier in the temperature-MBD relationship. Another one could be related to heat exposure differences that this study was not able to capture with ambient temperature estimates alone. For instance, in neighborhoods with the same ambient temperature estimated by our grid cells, those with more trees would have lower indoor temperatures due to shading than those with fewer trees. In other words, perhaps trees are capturing a temperature differential we cannot get using the current temperature data. The evidence is scarce for the potential moderating effect of greenness on the association between ambient temperature and mental health. One study reported that green space diminished the association between increasing temperatures and aggression in children and adolescents (Younan et al., 2018). Other studies have found that urban greenness was associated with improved mental health outcomes (Abraham Cottagiri et al., 2022). Recently, an ecological study found that increasing tree density and tree crown volume was associated with reductions in mood disorder medication sales in Brussels, Belgium (Chi et al., 2022).

Our findings that individuals with pre-existing mental health conditions are more likely to be at risk of MBD ED visits may help to explain potential pathways by which extreme heat may exacerbate MBDs. For instance, inherent conditions related to MBD and effects of psychiatric medications can affect impairment capacities and thermoregulatory control systems (Hwong et al., 2022; Hansen et al., 2008). Studies have shown that specific neurotransmitters related to thermoregulation may be affected during periods of extreme temperatures which affect dopaminergic transmissions and increase exacerbations of schyzophrenic episodes (Hasegawa et al., 1985; Sung et al., 2011). Psychotropic medications can also disrupt thermoregulatory processes and increase

vulnerability among individuals with MBDs (Shiloh et al., 2000; Conti et al., 2005). Specific medications that have been previously shown to affect thermoregulatory processes include anticholinergics, antidepressants, antihistamines (H3), mood stabilizers, antipsychotics, sedatives and antiepileptics (Martin-Latry et al., 2007). The inherent natural of MBDs can also affect individuals cognitive capacities during periods of extreme heat where people can neglect appropriate prevention measures such as staying hydrated, removing extra clothing and avoiding going outside (Hansen et al., 2008; Martin-Latry et al., 2007).

We also found that the impact of heat on MBD ED visits appeared highest when daily concontrations of NO2 and O3 were highest. Very few studies have investigated this issue. In a recent study in the U.S., Qiu et al. did not find any statistically significant interactions between different pollutant and warm temperature exposures (Qiu et al., 2022). Several studies have however found interactions between temperature and air pollutant exposures on cardiorespiratory morbidity and mortality outcomes (Anenberg et al., 2020). The mechanisms by which combined exposures to heat and air pollution exacerbates MBDs is not well understood. However, air pollutants have been previously shown to induce neuro-inflammatory responses which could trigger or worsen psychiatric conditions (Brun et al., 2012; Chu et al., 2019). Exposure to air pollution might also trigger MBDs by increasing glucocorticoid activity and stress hormone cortisol concentrations (Thomson et al., 2013; Tomei et al., 2003). Therefore, we hypothesize the combined exposures to mechanisms outlined above for heat with those of air pollution exposure might enchance the risk of MBDs. Further work is required in

This study has several strengths. The case-crossover study design is well suited for assessing the effects of transient risk factors (Maclure, 1991). We performed individual-level analyses of the associations between extreme temperatures and MBD ED visits. We took advantage of the postal code-linked ED visit data in order to assess neighborhood deprivation and residential environmental factors as effect modifiers.

This study has several limitations. First, we restricted our case selection to those receiving medical assistance for MBDs at the ED. Consequently, our findings cannot be generalized to cases not seeking care through the ED. Second, we identified pre-existing mental health conditions based on prior hospitalizations and ED visits which may only identify those individuals with more severe conditions. Some exposure misclassification is possible in this study if the cases did not spend time at the vicinity of their homes before the ED visit. Finally, we did not have individual-level data on race and socio-economic status (SES). Without these data, modification of the effect of extreme temperature by these individual-level factors could not be examined.

# 5. Conclusions

In summary, this case-crossover study provided evidence of an increased risk of ED visit for MBDs associated with short-term exposure to extreme heat. We also found differential effects according to neighborhood deprivation, residential greenness coverage, air pollution exposure and pre-existing mental health conditions. Additional research regarding the relationships between acute exposure to ambient temperature and MBD ED visits is needed, in particular in clarifying disparities in risks.

# Credit author statement

Eric Lavigne: Conceptualization, Writing- Original draft preparation, Methodology, Formal analysis; Writing- Reviewing and Editing; Alana Maltby: Writing- Reviewing and Editing; Jean-Nicolas Côté: Writing- Reviewing and Editing; Kate R. Weinberger: Writing-Reviewing and Editing; Christopher Hebbern: Writing- Reviewing and Editing; Methodology; Ana Maria Vicedo-Cabrera: Writing- Reviewing and Editing; Methodology; Piotr Wilk: Conceptualization; Writing-Reviewing and Editing; Methodology.

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# 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.

# Data availability

The authors do not have permission to share data.

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NDVI metrics, indexed to DMTI Spatial Inc. postal codes, were provided by CANUE; Tree Canopy metrics, indexed to DMTI Spatial Inc. postal codes, were provided by CANUE, Intellectual property rights to this dataset belong to University of Maryland, Department of Geographical Sciences and NASA; Local Climate Zone metrics, indexed to DMTI Spatial Inc. postal codes, were provided by CANUE.

# Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2022.114999.

# References

- Abraham Cottagiri, S., Villeneuve, P.J., Raina, P., et al., 2022. Increased urban greenness associated with improved mental health among middle-aged and older adults of the Canadian Longitudinal Study on Aging (CLSA). Environ. Res. 206, 112587 https://doi.org/10.1016/j.envres.2021.112587
- Anenberg, S.C., Haines, S., Wang, E., Nassikas, N., Kinney, P.L., 2020. Synergistic health effects of air pollution, temperature, and pollen exposure: a systematic review of epidemiological evidence. Environ. Health 19 (1), 130. https://doi.org/10.1186/ s12940-020-00681-z.
- Bateson, T.F., Schwartz, J., 2001. Selection bias and confounding in case-crossover analyses of environmental time-series data. Epidemiology 12 (6), 654–661. https://doi.org/10.1097/00001648-200111000-00013.
- Bechtel, B., Alexander, P.J., Böhner, J., et al., 2015. Mapping Local Climate Zones for a Worldwide Database of the Form and Function of Cities.
- Brook, J.R., Setton, E.M., Seed, E., Shooshtari, M., Doiron, D., Consortium CTCUEHR, 2018. The Canadian Urban Environmental Health Research Consortium - a protocol for building a national environmental exposure data platform for integrated analyses of urban form and health. BMC Publ. Health 18 (1), 114. https://doi.org/10.1186/ s12889-017-5001-5.
- Brun, E., Carriere, M., Mabondzo, A., 2012. In vitro evidence of dysregulation of blood-brain barrier function after acute and repeated/long-term exposure to TiO(2) nanoparticles. Biomaterials 33 (3), 886–896. https://doi.org/10.1016/j.biomaterials.2011.10.025.
- Bundo, M., de Schrijver, E., Federspiel, A., et al., 2021. Ambient temperature and mental health hospitalizations in Bern, Switzerland: a 45-year time-series study. PLoS One 16 (10), e0258302. https://doi.org/10.1371/journal.pone.0258302.
- Cakmak, S., Hebbern, C., Pinault, L., et al., 2018. Associations between long-term PM2.5 and ozone exposure and mortality in the Canadian Census Health and Environment Cohort (CANCHEC), by spatial synoptic classification zone. Environ. Int. 111, 200–211. https://doi.org/10.1016/j.envint.2017.11.030.
- CanMap Postal Code Suite v2015.3. Markam, 2015. DMTI Spatial Inc.
- Carlsen, H.K., Oudin, A., Steingrimsson, S., Oudin Astrom, D., 2019. Ambient temperature and associations with daily visits to a psychiatric emergency unit in Sweden. Int. J. Environ. Res. Publ. Health 16 (2). https://doi.org/10.3390/ ijerph16020286.
- Chi, D., Aerts, R., Van Nieuwenhuyse, A., et al., 2022. Residential exposure to urban trees and medication sales for mood disorders and cardiovascular disease in Brussels, Belgium: an ecological study. Environ. Health Perspect. 130 (5), 57003 https://doi. org/10.1289/EHP9924.
- Chu, C., Zhang, H., Cui, S., et al., 2019. Ambient PM2.5 caused depressive-like responses through Nrf2/NLRP3 signaling pathway modulating inflammation. J. Hazard Mater. 369, 180–190. https://doi.org/10.1016/j.jhazmat.2019.02.026.

- Cianconi, P., Betrò, S., Janiri, L., 2020. The impact of climate change on mental health: a systematic descriptive review. Front. Psychiatr. 11, 74. https://doi.org/10.3389/ fpsyt.2020.00074. PMID: 32210846; PMCID: PMC7068211.
- Conti, S., Meli, P., Minelli, G., et al., 2005. Epidemiologic study of mortality during the Summer 2003 heat wave in Italy. Environ. Res. 98 (3), 390–399. https://doi.org/ 10.1016/j.envres.2004.10.009.
- DMTI Spatial Inc. CanMap Postal Code Suite V2010 and V2015.
- Ebi, K.L., Vanos, J., Baldwin, J.W., et al., 2021a. Extreme weather and climate change: population health and health system implications. Annu. Rev. Publ. Health 42, 293–315. https://doi.org/10.1146/annurev-publhealth-012420-105026.
- Ebi, K.L., Capon, A., Berry, P., et al., 2021b. Hot weather and heat extremes: health risks. Lancet 398 (10301), 698–708. https://doi.org/10.1016/s0140-6736(21)01208-3.
- Environment Canada, 2022. National Air Pollution Surveillance Program. Statistics

  Canada. https://www.canada.ca/en/environment-climate-change/services/air-poll
  ution/monitoring-networks-data/national-air-pollution-program.html.
- Gamache, P., Hamel, D., Blaser, C., 2019. Material and Social Deprivation Index: A Summary –INSPQ Website. www.inspq.qc.ca/en/publications/2639.
- Gasparrini, A., 2014. Modeling exposure-lag-response associations with distributed lag non-linear models. Stat. Med. 33 (5), 881–899. https://doi.org/10.1002/sim.5963.
- Gasparrini, A., Guo, Y., Hashizume, M., et al., 2015. Mortality risk attributable to high and low ambient temperature: a multicountry observational study. Lancet 386 (9991), 369–375. https://doi.org/10.1016/s0140-6736(14)62114-0.
- Gibson, D., Richards, H., Chapman, A., 2008. The National Ambulatory Care Reporting System: factors that affect the quality of its emergency data. Int. J. Inf. Qual. 2 (2) https://doi.org/10.1504/ijiq.2008.022958.
- Gorelick, N., Hancher, M., Dixon, M., Ilyushchenko, S., Thau, D., Moore, R., 2017. Google earth engine: planetary-scale geospatial analysis for everyone. Rem. Sens. Environ. 202, 18–27. https://doi.org/10.1016/j.rse.2017.06.031.
- Hansen, A., Bi, P., Nitschke, M., Ryan, P., Pisaniello, D., Tucker, G., 2008. The effect of heat waves on mental health in a temperate Australian city. Environ. Health Perspect. 116 (10), 1369–1375. https://doi.org/10.1289/ehp.11339.
- Hasegawa, H., Ishiwata, T., Saito, T., Yazawa, T., Aihara, Y., Meeusen, R., 1985. Inhibition of the preoptic area and anterior hypothalamus by tetrodotoxin alters thermoregulatory functions in exercising rats. J. Appl. Physiol. 98 (4), 1458–1462. https://doi.org/10.1152/japplphysiol.00916.2004. Apr 2005.
- Henderson, S.B., McLean, K.E., Lee, M.J., Kosatsky, T., 2022. Analysis of community deaths during the catastrophic 2021 heat dome: early evidence to inform the public health response during subsequent events in greater Vancouver, Canada. Environ Epidemiol 6 (1), e189. https://doi.org/10.1097/EE9.0000000000000189.
- Heo, S., Chen, C., Kim, H., et al., 2021. Temporal Changes in Associations between High Temperature and Hospitalizations by Greenspace: Analysis in the Medicare Population in 40 U.S. Northeast Counties. Environment International, 156106737. https://doi.org/10.1016/j.envint.2021.106737. Article.
- Ho, H.C., Knudby, A., Chi, G., Aminipouri, M., Yuk-FoLai, D., 2018. Spatiotemporal analysis of regional socio-economic vulnerability change associated with heat risks in Canada. Appl. Geogr. 95, 61–70. https://doi.org/10.1016/j.apgeog.2018.04.015.
- Hwong, A.R., Wang, M., Khan, H., et al., 2022. Climate change and mental health research methods, gaps, and priorities: a scoping review. Lancet Planet. Health 6 (3), e281–e291. https://doi.org/10.1016/S2542-5196(22)00012-2.
- Jaakkola, J.J., 2003. Case-crossover design in air pollution epidemiology. Eur. Respir. J. Suppl. 40, 81s-85s. https://doi.org/10.1183/09031936.03.00402703.
- Janes, H., Sheppard, L., Lumley, T., 2005. Case-crossover analyses of air pollution exposure data: referent selection strategies and their implications for bias. Epidemiology 16 (6), 717–726. https://doi.org/10.1097/01. ede.0000181315.18836.9d.
- Jay, O., Capon, A., Berry, P., et al., 2021. Reducing the health effects of hot weather and heat extremes: from personal cooling strategies to green cities. Lancet 398 (10301), 709–724. https://doi.org/10.1016/S0140-6736(21)01209-5.
- Lavigne, E., Gasparrini, A., Wang, X., et al., 2014. Extreme ambient temperatures and cardiorespiratory emergency room visits: assessing risk by comorbid health conditions in a time series study. Article. *Environmental Health: A Global Access Science Source*. 13 (1), 5. https://doi.org/10.1186/1476-069X-13-5.
- Lee, S., Lee, H., Myung, W., Kim, E.J., Kim, H., 2018. Mental disease-related emergency admissions attributable to hot temperatures. Sci. Total Environ. 688–694. https:// doi.org/10.1016/j.scitotenv.2017.10.260, 616-617.
- Levy, D., Lumley, T., Sheppard, L., Kaufman, J., Checkoway, H., 2001. Referent selection in case-crossover analyses of acute health effects of air pollution. Epidemiology 12 (2), 186–192. https://doi.org/10.1097/00001648-200103000-00010.
- Linares, C., Culqui, D., Carmona, R., Ortiz, C., Díaz, J., 2017. Short-term association between environmental factors and hospital admissions due to dementia in Madrid. Environ. Res. 152, 214–220. https://doi.org/10.1016/j.envres.2016.10.020.
- Ma, Y., Zhou, L., Chen, K., 2020. Burden of cause-specific mortality attributable to heat and cold: a multicity time-series study in Jiangsu Province, China. Environ. Int. 144, 105994 https://doi.org/10.1016/j.envint.2020.105994.
- Maclure, M., 1991. The case-crossover design: a method for studying transient effects on the risk of acute events. Am. J. Epidemiol. 133 (2), 144–153. https://doi.org/ 10.1093/oxfordjournals.aje.a115853.
- Martin-Latry, K., Goumy, M.P., Latry, P., et al., 2007. Psychotropic drugs use and risk of heat-related hospitalisation. Eur. Psychiatr. 22 (6), 335–338 doi:S0924-9338(07) 01308-9 [pii].
- Mullins, J.T., White, C., 2019. Temperature and mental health: evidence from the spectrum of mental health outcomes. J. Health Econ. 68, 102240 https://doi.org/ 10.1016/j.jhealeco.2019.102240.
- Navidi, W., Weinhandl, E., 2002. Risk set sampling for case-crossover designs.

  Epidemiology 13 (1), 100–105. https://doi.org/10.1097/00001648-200201000-00016

- Niu, Y., Gao, Y., Yang, J., et al., 2020. Short-term effect of apparent temperature on daily emergency visits for mental and behavioral disorders in Beijing, China: a time-series study. Sci. Total Environ. 733, 139040 https://doi.org/10.1016/j. scitotenv.2020.139040.
- Nori-Sarma, A., Sun, S., Sun, Y., et al., 2022. Association between ambient heat and risk of emergency department visits for mental health among US adults, 2010 to 2019. JAMA Psychiatr. 79 (4), 341–349. https://doi.org/10.1001/ jamapsychiatry.2021.4369.
- Pampalon, R., Hamel, D., Gamache, P., Philibert, M.D., Raymond, G., Simpson, A., 2012.
  Un indice régional de défavorisation matérielle et sociale pour la santé publique au Québec et au Canada. Can. J. Public Health 103 (S2), S17–S22. https://doi.org/10.1007/bf03403824
- Qiu, X., Danesh-Yazdi, M., Wei, Y., et al., 2022. Associations of short-term exposure to air pollution and increased ambient temperature with psychiatric hospital admissions in older adults in the USA: a case-crossover study. Lancet Planet. Health 6 (4), e331–e341. https://doi.org/10.1016/S2542-5196(22)00017-1.
- Robinson, N., Allred, B., Jones, M., et al., 2017. A dynamic Landsat derived normalized difference vegetation index (NDVI) product for the conterminous United States. Rem. Sens. 9 (8) https://doi.org/10.3390/rs9080863.
- Romanello, M., McGushin, A., Di Napoli, C., et al., 2021. The 2021 report of the Lancet Countdown on health and climate change: code red for a healthy future. Lancet 398 (10311), 1619–1662. https://doi.org/10.1016/s0140-6736(21)01787-6.
- Schwartz, J., 2004. The effects of particulate air pollution on daily deaths: a multi-city case crossover analysis. Occup. Environ. Med. 61 (12), 956–961. https://doi.org/ 10.1136/oem.2003.008250.
- Sera, F., Armstrong, B., Tobias, A., et al., 2019a. How urban characteristics affect vulnerability to heat and cold: a multi-country analysis. Int. J. Epidemiol. 48 (4), 1101–1112. https://doi.org/10.1093/ije/dyz008.
- Sera, F., Armstrong, B., Blangiardo, M., Gasparrini, A., 2019b. An extended mixed-effects framework for meta-analysis. Stat. Med. 38 (29), 5429–5444. https://doi.org/ 10.1002/sim.8362.
- Sexton, J.O., Song, X.-P., Feng, M., et al., 2013. Global, 30-m resolution continuous fields of tree cover: Landsat-based rescaling of MODIS vegetation continuous fields with lidar-based estimates of error. International Journal of Digital Earth 6 (5), 427–448. https://doi.org/10.1080/17538947.2013.786146.
- Shiloh, R., Hermesh, H., Weizer, N., Dorfman-Etrog, P., Weizman, A., Munitz, H., 2000. Acute antipsychotic drug administration lowers body temperature in drug-free male schizophrenic patients. Eur. Neuropsychopharmacol 10 (6), 443–445. https://doi.org/10.1016/s0924-977x(00)00106-1.
- Son, J.Y., Choi, H.M., Miranda, M.L., Bell, M.L., 2022. Exposure to heat during pregnancy and preterm birth in North Carolina: main effect and disparities by residential greenness, urbanicity, and socioeconomic status. Environ. Res. 204 (Pt C), 112315 https://doi.org/10.1016/j.envres.2021.112315.
- Statistics Canada, 2017. Population Ecumene Census Division Cartographic Boundary File, Reference Guide, 2016 Census. https://www150.statcan.gc.ca/n1/pub/92-159-g/92-159-g2016001-eng.htm.
- Statistics Canada, 2021. Health characteristics, two-year period estimates. https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1310011301.
- Stieb, D.M., Evans, G.J., To, T.M., Brook, J.R., Burnett, R.T., 2020. An ecological analysis of long-term exposure to PM2.5 and incidence of COVID-19 in Canadian health regions. Environ. Res. 191, 110052 https://doi.org/10.1016/j.envres.2020.110052.
- Sung, T.I., Chen, M.J., Lin, C.Y., Lung, S.C., Su, H.J., 2011. Relationship between mean daily ambient temperature range and hospital admissions for schizophrenia: results from a national cohort of psychiatric inpatients. Sci. Total Environ. 410–411, 41–46. https://doi.org/10.1016/j.scitotenv.2011.09.028.

- Thomson, E.M., Vladisavljevic, D., Mohottalage, S., Kumarathasan, P., Vincent, R., 2013. Mapping acute systemic effects of inhaled particulate matter and ozone: multiorgan gene expression and glucocorticoid activity. Toxicol. Sci. 135 (1), 169–181. https://doi.org/10.1093/toxsci/kft137.
- Thornton, P.E., Shrestha, R., Thornton, M., Kao, S.C., Wei, Y., Wilson, B.E., 2021. Gridded daily weather data for North America with comprehensive uncertainty quantification. Sci. Data 8 (1), 190. https://doi.org/10.1038/s41597-021-00973-0.
- Tomei, F., Rosati, M.V., Ciarrocca, M., et al., 2003. Plasma cortisol levels and workers exposed to urban pollutants. Ind. Health 41 (4), 320–326. https://doi.org/10.2486/ indhealth.41.320.
- USGS Landsat 5 TM TOA Reflectance (Orthorectified), 1984 to, 2011. https://explorer.earthengine.google.com/detail/LANDSAT/LT5\_L1T\_TOA.
- DMTI Spatial Inc, 2015. v2015.3 Data: CanMap Content Suite, [CanMap Postal Suite] V1.

  Deposited 2015-01-01. doi:hdl/11272.1/AB2/WZOPIP. No volume and page available
- USGS Landsat 8 TOA Reflectance (Orthorectified), 2013 to 2017. Accessed July, 2017. https://explorer.earthengine.google.com/detail/LANDSAT/LC8\_L1T\_TOA.
- Wang, X., Lavigne, E., Ouellette-Kuntz, H., Chen, B.E., 2014. Acute impacts of extreme temperature exposure on emergency room admissions related to mental and behavior disorders in Toronto, Canada. Article. J. Affect. Disord. 155 (1), 154–161. https://doi.org/10.1016/j.jad.2013.10.042.
- Wei, Y., Wang, Y., Lin, C.K., et al., 2019. Associations between seasonal temperature and dementia-associated hospitalizations in New England. Environ. Int. 126, 228–233. https://doi.org/10.1016/j.envint.2018.12.054.
- Williams, P.D., Ambaum, M.H.P., 2021. Chapter 5 water in the atmosphere. In: Developments in Weather and Climate Science. Thermal Physics of the Atmosphere, second ed. ed. Elsevier, pp. 91–114.
- Xu, R., Zhao, Q., Coelho, M., et al., 2020. Socioeconomic inequality in vulnerability to all-cause and cause-specific hospitalisation associated with temperature variability: a time-series study in 1814 Brazilian cities. Lancet Planet. Health 4 (12), e566–e576. https://doi.org/10.1016/S2542-5196(20)30251-5.
- Xu, R., Xiong, X., Abramson, M.J., Li, S., Guo, Y., 2021. Association between ambient temperature and sex offense: a case-crossover study in seven large US cities, 2007–2017. Sustain. Cities Soc. 69, 102828 https://doi.org/10.1016/j. scs.2021.102828.
- Ye, X., Wolff, R., Yu, W., Vaneckova, P., Pan, X., Tong, S., 2012. Ambient temperature and morbidity: a review of epidemiological evidence. Environ. Health Perspect. 120 (1), 19–28. https://doi.org/10.1289/ehp.1003198.
- Yi, W., Zhang, X., Gao, J., et al., 2019. Examining the association between apparent temperature and admissions for schizophrenia in Hefei, China, 2005-2014: a timeseries analysis. Sci. Total Environ. 672, 1–6. https://doi.org/10.1016/j. scitotenv.2019.03.436.
- Yoo, E.H., Eum, Y., Gao, Q., Chen, K., 2021a. Effect of extreme temperatures on daily emergency room visits for mental disorders. Environ. Sci. Pollut. Res. Int. 28 (29), 39243–39256. https://doi.org/10.1007/s11356-021-12887-w.
- Yoo, E.H., Eum, Y., Roberts, J.E., Gao, Q., Chen, K., 2021b. Association between extreme temperatures and emergency room visits related to mental disorders: a multi-region time-series study in New York, USA. Sci. Total Environ. 792, 148246 doi:S0048-9697 (21)03317-9.
- Younan, D., Li, L., Tuvblad, C., et al., 2018. Long-term ambient temperature and externalizing behaviors in adolescents. Am. J. Epidemiol. 187 (9), 1931–1941. https://doi.org/10.1093/aje/kwy104.
- Zhang, S., Yang, Y., Xie, X., et al., 2020. The effect of temperature on cause-specific mental disorders in three subtropical cities: a case-crossover study in China. Environ. Int. 143, 105938 https://doi.org/10.1016/j.envint.2020.105938.