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A population-based case-control analysis of risk factors associated with mortality during the 2021 western North American heat dome: focus on chronic conditions and social vulnerability

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Abstract

Western North America experienced an unprecedented extreme heat event (EHE) in early summer 2021. In the province of British Columbia (BC), this event was associated with an estimated 740 excess deaths, making it one of the deadliest weather events in Canadian history. This study uses a population-based case-control design to compare 1597 adults (cases) who died during the EHE (25 June–2 July 2021) with 7968 similar adults (controls) who survived. The objective was to identify risk factors for death during the EHE by examining differences in chronic diseases and social vulnerability between the cases and controls. We used care setting, age category, sex, and geographic area of cases to identify comparable surviving controls. We used logistic regression to estimate the odds ratio (OR) for each chronic disease, adjusted for care setting, age category, sex, and geographic area. We further adjusted for individual-level low-income status to identify changes in the estimated ORs with the addition of this indicator of social vulnerability. The risk factor most strongly associated with EHE mortality was individual-level low income. The fully adjusted OR [95% confidence interval] for receiving income assistance was 2.42 [1.98, 2.95]. The chronic disease most strongly associated with EHE mortality was schizophrenia, with a fully adjusted OR of 1.93 [1.51, 2.45]. Chronic obstructive pulmonary disease, parkinsonism, heart failure, chronic kidney disease, ischemic stroke, and substance use disorder were also associated with significantly higher odds of EHE mortality. These results confirm the roles of social vulnerability, mental illness, and other specific underlying chronic conditions (renal, respiratory, cardiovascular, cerebrovascular, and neurological) in risk of mortality during EHEs. This information is being used to inform policy and planning to reduce risk during future EHEs in BC and across Canada.

1. Introduction

Extreme heat events (EHEs) occur worldwide, and they can cause significant population mortality. EHEs in Russia [1, 2], India [3], the United States (US) [4], and multiple countries in Europe [5] have each resulted in excess deaths numbering in the hundreds to tens of thousands. The most extreme examples include prolonged EHEs in Europe in 2003 and in Russia in 2010, which resulted in an estimated 70 000 and 55 000 excess deaths, respectively [2]. In the absence of effective adaptation measures, the burden of global EHE-related mortality is expected to increase markedly in the coming decades as the climate changes and EHEs continue to become more frequent and severe [6, 7]. Thus, it remains critical to clarify the impacts of EHEs on mortality to inform effective adaptation strategies to reduce their future burden.

People are not equally susceptible to dying during EHEs. Therefore, deaths during these events may be concentrated among certain groups. For example, older age and diabetes are widely recognized as risk factors for greater susceptibility to extreme heat because they affect physiological thermoregulation [8, 9]. Other well-documented risk factors include cardiovascular conditions, respiratory disease, and mental illness [10, 11]. However, greater susceptibility is also linked to non-physiological factors including social vulnerability, features of the built environment, and behavioral adaptation. For instance, during hot weather from 1997 to 2006 in New York City, deaths among older individuals were concentrated in areas with higher levels of poverty, poorer housing conditions, and lower access to air conditioning [12]. Similarly, during the 1995 heat wave in Chicago, risk factors for mortality included being confined to a bed with a medical condition, lacking access to transportation, and being socially isolated with fewer social contacts and living alone [4].

Susceptibility to extreme heat is not determined by any single factor, but rather depends on the confluence of overlapping factors. For example, higher social vulnerability is associated with several risk factors for EHE mortality, including a higher prevalence of chronic diseases, poorer overall health, lower access to air conditioning, and features of the built environment that promote higher local temperatures such as lower greenspace and more paved surfaces [13–16]. People living in different regions of the world also experience different risks. For example, populations at higher latitudes, where heat has been less common historically, tend to experience higher mortality rates starting at cooler temperatures due to lower physiological and behavioral adaptation to heat [17]. Further, risks vary with EHE-specific conditions including maximum daytime and nighttime temperatures, humidity, event duration, and co-occurrence with other environmental exposures such as wildfire smoke and ground-level ozone [1, 18]. As such, it is important to establish risks locally for specific EHEs to identify at-risk groups that can be targeted for public health interventions during future events.

In early summer 2021, western North America experienced an unprecedented EHE. In the province of British Columbia (BC), Canada, this event was associated with a 95% increase in population mortality (an estimated 740 excess deaths), making it one of the deadliest weather events in Canadian history [13, 19, 20]. As part of concerted efforts to understand the health impacts of this EHE, the BC Centre for Disease Control (BCCDC) has already conducted two studies. One examined all deaths across the province, and found elevated mortality among individuals with schizophrenia, chronic kidney disease, and ischemic heart disease [21]. The other examined all community deaths in the greater Vancouver region and found elevated mortality among those living in neighborhoods with higher levels of social and material deprivation and lower levels of greenspace [13]. Both studies used a case-only design, comparing people who died during the EHE with those who died during more typical summer weather in previous years.

The case-only design is convenient and efficient because subjects can be identified using death records alone. While the case-only design provides information on how people who died during the EHE differed from people who died at other times, it does not provide information on how people who died during the EHE differed from those who survived. For example, in Lee *et al* [21] we did not find an association between heart failure and mortality during the 2021 EHE, though cardiovascular disease is a well-established risk factor for hot weather death [22–25]. This disparity between our study and the wider literature may be due to using decedents as the comparator group, because cardiovascular disease is a common condition among people who die. To address this gap in our prior analyses for BC and to generate evidence more comparable with other case-control studies conducted on mortality during EHEs, this study adds critical evidence to the case-only analyses in two important ways. First, it identifies risk factors for death using a population-based case-control design, comparing characteristics of people who died during the EHE with similar people who survived. Second, it estimates the effects of both health and social risk factors including chronic disease and individual-level low-income status.

2. Methods

2.1. Study setting

BC is the westernmost province in Canada. It has a mountainous landmass of nearly one million km^2 with many large and small islands and an extensive Pacific coastline. The spatial variability of weather and climate in BC is influenced by its complex topography and its wide range of latitude and longitude. The south-eastern region has hotter summers (median high of 27 °C for July–August 2012–2020) than the rest of the province (median high of 21 °C for July–August 2012–2020). The south-eastern region also has a higher prevalence of household air conditioning, while many homes in the rest of the province do not have air conditioning [26]. BC had a population of approximately 5.2 million people in 2021, with about 60% (∼3.05 million) living in the greater Vancouver region located on the southwest coast of the province [27].

During western North America's 2021 EHE, temperatures began increasing on 24 June, days after the annual peak of daylight hours at the summer solstice [20]. This EHE was caused by a meteorological

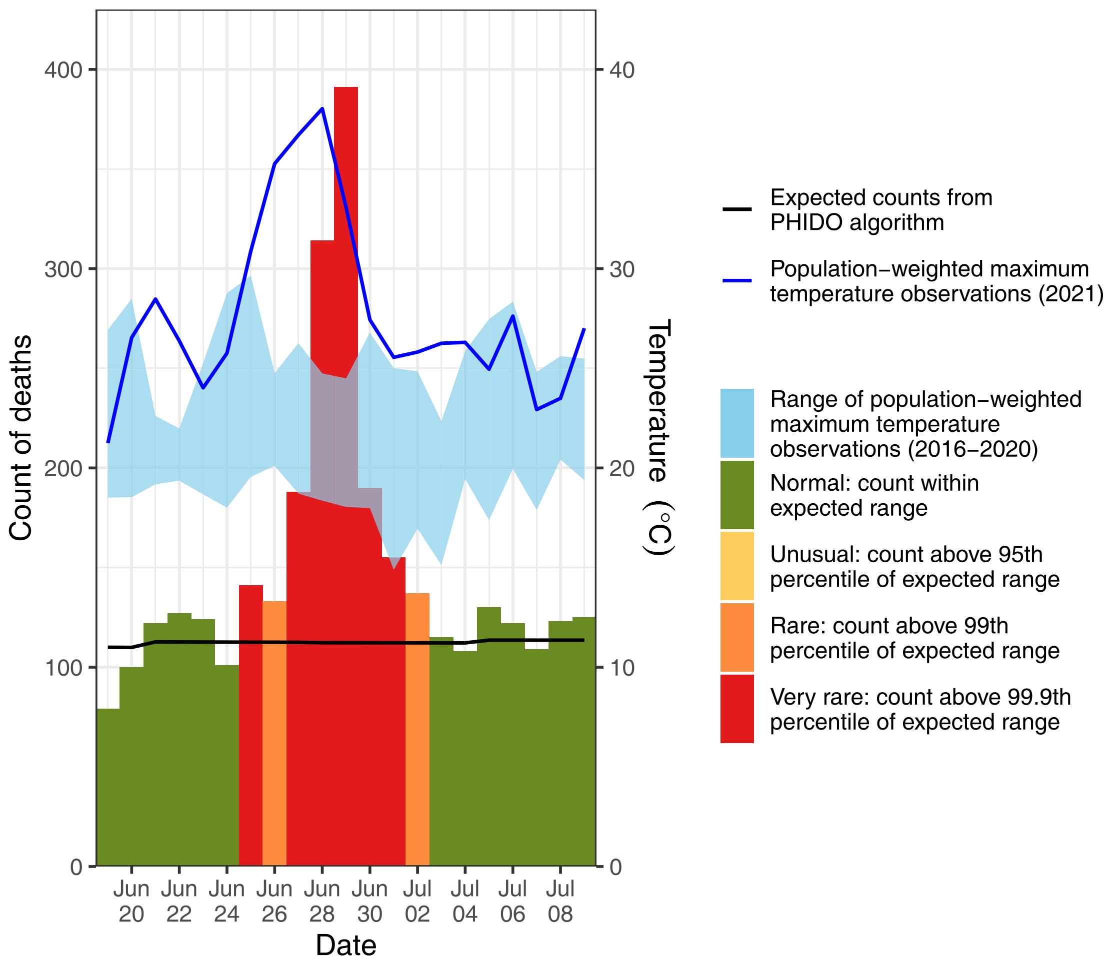

Figure 1. Daily counts of deaths (bars) and population-weighted averages of daily maximum temperature observations (dark blue line) in 2021. The range of daily population-weighted maximum temperature observations from 2016 to 2020 (light blue ribbon) shows the difference between temperatures in 2021 compared with seasonal norms. Bars are colored according to the degree of statistical deviation from the daily expected counts (black line) calculated using the Public Health Intelligence for Disease Outbreaks (PHIDO) algorithm. PHIDO is used by the British Columbia Centre for Disease Control to detect anomalies. The EHE was defined as the 8-day period when there was statistically significant excess mortality (orange and red bars) in the province (25 June–2 July 2021).

phenomenon known as a 'heat dome', which occurs when a high-pressure system gets caught in an atmospheric blocking pattern, trapping heat near the earth's surface for an extended period [20, 28]. Air temperatures across BC were unprecedented between 25 June and 2 July 2021, reaching 16 °C–20°C above seasonal norms (figure 1) [20]. Elevated concentrations of ground-level ozone and fine particulate matter co-occurred in some regions [21], prompting an extended air quality advisory in greater Vancouver [13]. For these and other analyses, we have considered the overall impacts of the EHE period without the objective of separating the contributions of heat and air pollution exposure to population mortality. Consistent with our prior analyses [13, 21], we defined the EHE period as the eight days (25 June–2 July 2021) with statistically significant excess mortality across BC that coincided with the anomalous air temperatures (figure 1). To establish this period, we generated excess mortality estimates using the Public Health Intelligence for Disease Outbreaks (PHIDO) algorithm to model expected deaths based on data from the past five years, and then compared observed deaths with the expected range [13, 21]. PHIDO was developed by the BCCDC for anomaly detection in the early 2000s, and has formed the basis of all public health surveillance at the BCCDC for more than 20 years.

2.2. Study design and administrative health data

This population-based case-control study compares adults (>18 years) who died in BC during the EHE with similar adults who survived the EHE. We used administrative health data from multiple datasets to select the cases, controls, and covariates used in the analyses. All datasets are included in the BC COVID-19 Data Library, which was established to support public health response during the pandemic [29]. The Medical Services Plan (MSP) is the provincial single-payer healthcare insurance program, and everyone enrolled in

Table 1. Description of administrative health datasets used in the study for subject selection and analysis.

Dataset name	Description	Used in study for
Vital Statistics	Death records for all deaths in BC	Subject selection
Client Roster	Best available demographic and geographic information for BC Ministry of Health Medical Services Plan (MSP) registrants	Subject selection
Discharge Abstract Database (DAD)	Information on hospital discharges, transfers and deaths of in-patients and day surgery patients from acute care hospitals in BC	Subject selection
National Ambulatory Care Reporting System (NACRS)	Information on hospital-based and community-based ambulatory care including day surgery, outpatient and community-based clinics, and emergency departments	Subject selection
Health System Matrix	BC Ministry of Health tool used to understand healthcare needs and estimate costs to the healthcare system, in which information from multiple databases is used to assign BC residents to population segments that represent their healthcare needs based on diagnoses or use of specific services	Subject selection
PharmaNet	All prescriptions dispensed in community pharmacies in BC, including whether the prescription was dispensed under a BC PharmaCare plan	Subject selection and analysis
Medical Services Plan (MSP)	Information on out-patient medical and healthcare services covered under the province's public health insurance	Subject selection
Immunizations Registry	Information on COVID-19 vaccinations	Subject selection
Chronic Disease Registries	26 administrative chronic disease registries based on individual patterns of healthcare usage	Analysis

the MSP has a unique patient identifier. The COVID-19 Data Library includes individual-level anonymized health records from multiple administrative datasets that can be linked using the unique patient identifier. The BCCDC obtained authorization from the BC Ministry of Health to use the COVID-19 Data Library to generate evidence about the public health impacts of the EHE. This work is included in the mandate of the BCCDC under the BC Public Health Act and as per BC legislation does not require informed consent. As per the Tri-Council Policy Statement Ethical Conduct for Research Involving Humans, this project and the data used to support it, are Research Ethics Board exempt [30]. We used data from 9 different sources within the COVID-19 Data Library (table 1).

2.3. Study subjects

We identified cases by extracting all records with a death date during the EHE (25 June–2 July 2021) from the vital statistics data. Deaths among children ($\leqslant$18 years) were excluded because the BC Coroners Service (Coroners Service) reported that all heat-related deaths during the 2021 EHE occurred among adults [31]. Death records were linked to the MSP client roster to add demographic and geographic information. Cases that had missing information on age, sex, or residential location were excluded (figure 2). Cause of death information was incomplete in the vital statistics data at the time of the study, so we did not consider it in the case definition or the analysis.

The pool of potential controls included the entire adult population of MSP clients who (1) survived the EHE for at least 60 d and (2) had complete information on age, sex, and residential location available in the client roster at the time of data extraction (10 November 2022). The Coroners Service reported that following injury during the 2021 EHE, the heat-related deaths occurred over a seven-month period, but 562 (91%) died during our defined EHE period and over 96% died within 10 d of the EHE [31]. Given the delayed onset of death from injuries associated with the EHE, we chose the first criterion of 60 d to ensure that most heat-related deaths were excluded from the pool of potential controls. We used characteristics of the cases to select controls to improve analytical efficiency by having similar numbers of cases and controls with each combination of these characteristics [32]. Controls were selected based on the combination of four factors (1) care setting during the EHE; (2) age category; (3) sex; and (4) health region of residence. First, we assigned each case and potential control to a unique group based on their combination of these four factors. Next, for each case in the group, we randomly selected up to five controls from the pool of potential controls in that

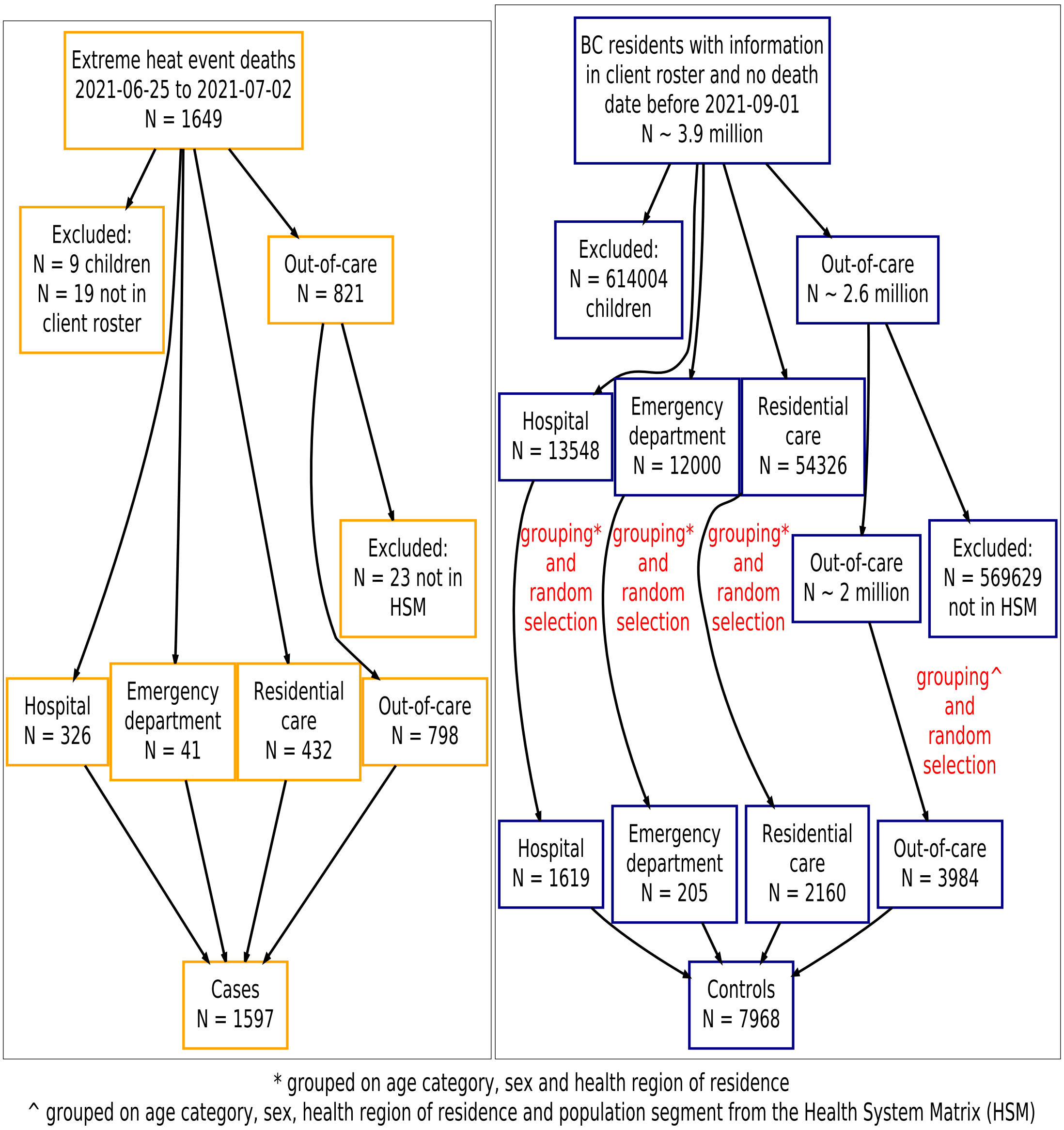

Figure 2. Flow chart of extreme heat event (EHE) deaths (cases; left panel) and survivors (controls; right panel) included in the study. After excluding children and adults with missing data, we assigned cases and potential controls to the likely care setting of each individual during the EHE. We randomly selected up to five controls per case from the pool of potential controls within each unique combination of care setting, age category, sex and health region of residence. Population segments from the Health System Matrix (HSM) were also used in the selection process for the out-of-care group.

group (figure 2). We chose this 5:1 ratio of controls per case to balance maximizing statistical precision while minimizing the number of strata with insufficient controls [33]. We chose not to assign individual controls to individual cases, as would be done in a conditional analysis, based on data published in Pearce [32] showing that a standard unconditional analysis can be more precise and equally valid as conditional analysis.

More specifically, the first step in the subject selection process was to assign individuals to their likely care setting during the EHE. We included care setting as a grouping factor for subject selection because there is a different overall risk of mortality associated with each care setting regardless of the presence of an EHE (e.g. residential care versus out-of-care). By including care setting as a grouping factor, we ensured a balance in the number of cases and controls from each care setting in the analysis. We assigned cases and potential controls to one of the following care settings based on indicators in administrative health datasets:

1. *Residential care* Individuals were assigned to residential care if there was any indicator of their being in residential care in the year prior to the EHE. The five indicators (table A.1) considered were (1) record of hospital discharge (DAD) to residential care; (2) prescription (PharmaNet) dispensed to a residential care facility; (3) out-patient healthcare service (MSP) provided at a residential care facility; (4) living in

residential care according to the Health System Matrix; and/or (5) COVID-19 immunization provided to an individual living in residential care.

2. *Hospital inpatient care* Individuals were assigned to hospital inpatient care if (1) they were not assigned to residential care and (2) they had at least one entry in the DAD that overlapped with the EHE period.
3. *Emergency department (ED) care* Individuals were assigned to ED care if (1) they were not assigned to residential care or hospital care and (2) they had at least one entry in NACRS that overlapped with the EHE period.
4. *Out-of-care* Finally, individuals were assigned to out-of-care if they were not previously assigned to any of the other care settings.

After assigning the care setting, we grouped on age category, sex, and health region of residence using BC's 16 Health Service Delivery Areas [34]. We assigned cases and potential controls to age categories using their age during the EHE. We used slightly different age categories for each care setting based on the availability of potential controls (table A.2). We included age category and sex as grouping factors because both age and sex are associated with risk of mortality regardless of the presence of an EHE. In addition, there were anomalous temperatures across BC during the EHE, but the degree of anomaly differed by region. We included health region of residence as a grouping factor because of these differences in climatic experience, and because other factors that impact risk of EHE mortality differ by region such as access to and use of healthcare services [35] and prevalence of household air conditioning [26].

Finally, we used the population segments from the Health System Matrix in the selection process for the out-of-care group. The Health System Matrix is a tool used to understand healthcare needs and estimate costs to the healthcare system in BC (table 1). Within this tool, information from multiple databases is used to assign BC residents to population segments that represent their healthcare needs based on diagnoses or use of specific services. Compared with the other care setting groups, the entire pool of potential controls assigned to the out-of-care group was significantly larger and had greater variability in health status and risk of mortality. We used the population segments as a grouping factor for the out-of-care group to make the cases and controls more comparable in terms of their baseline risk of death prior to the EHE. Individuals can be assigned to more than one population segment, and we used the highest-need segment for each case and potential control. The Health System Matrix for the 2018–2019 fiscal year (April to March) was the most recent version available, and any individuals assigned to the out-of-care group with no information in the Health System Matrix for that year were excluded from the study (figure 2). No information in the Health System Matrix means the individual was not registered in the MSP during that year.

2.4. Chronic diseases

The BC Ministry of Health maintains administrative registries of 26 chronic diseases to monitor their incidence and prevalence over time. Individuals are added to one or more registries based on their patterns of healthcare usage. The case definitions vary by disease, considering hospitalization diagnoses, physician services diagnoses, and pharmaceutical dispensations [36]. The most recent versions of the chronic disease registries available in the COVID-19 Data Library included incidence dates through 31 March 2020. If a study subject had an incidence date in a registry, we considered that disease to be present, and otherwise we considered it to be absent. We also classified subjects by their total number of chronic diseases (0, 1–2, 3–6, and 7+) to assess the odds of EHE mortality with increasing multi-morbidity (see section A.1 in the supplementary appendix).

We included 22 of the 26 chronic disease registries in the analyses. We excluded the juvenile arthritis registry, which only covers children <16 years of age. We also excluded the hemorrhagic stroke and multiple sclerosis registries because <1% of the cases were included in each. Some of the registries cover a broad range of conditions, and individuals with more specific conditions are included in both the higher-level registry and a more specific subset registry [36]. We excluded or modified three of these higher-level registries. The hospitalized stroke registry was excluded because it includes all patients in the three subset stroke registries. All individuals in the depression registry are also in the mood and anxiety disorders registry. We modified the mood and anxiety disorders registry by removing patients also in the depression registry such that the remaining patients have mood or anxiety disorder(s) without depression. Similarly, because all people in the angina registry are also in the ischemic heart disease registry, we created two separate categories for ischemic heart disease with and without angina.

2.5. Social vulnerability

We assessed social vulnerability using the BC Ministry of Health's PharmaCare Plan C (Plan C) as a proxy for individual-level low-income status in the study population. Plan C covers 100% of prescription costs for individuals enrolled in the BC Employment and Assistance program. We extracted all prescriptions dispensed within a one-year period ending on 2 July 2021 from the PharmaNet database. Individuals who had one or more dispensations covered by Plan C during that time were classified as such and assumed to be low income. Individuals were classified as having unknown Plan C coverage if they had no prescriptions dispensed during the year preceding the EHE (<10%). All others were classified as not being covered by Plan C. In addition, we assessed social vulnerability using a neighborhood-level deprivation index called the Canadian Index of Multiple Deprivation (CIMD) (see section A.2 in the supplementary appendix).

2.6. Statistical analysis

Data were extracted using R version 3.6.2 (2019-12-12) and analyzed using R version 4.2.0 (2022-04-22) [37]. We fit logistic regression models to describe the relationship between EHE mortality, chronic diseases, and an indicator of social vulnerability. We report ORs to quantify the associations between case status and presence of each chronic disease adjusted for all other chronic diseases (equation 1).

$$\text{case status} = \text{chronic disease}_1 + \text{chronic disease}_2 + \ldots + \text{chronic disease}_{22} + \text{age} + \text{sex} + \text{region} + \text{care setting}. \quad (1)$$

We extended the model represented in equation (1) by adding a covariate indicating individual-level low income (Plan C) (equation (2)). We included the grouping variables used during subject selection as independent variables in both adjusted models to reduce selection bias or other biases introduced by the selection process [32, 38].

$$\begin{aligned}\text{case status} = {} & \text{chronic disease}_1 + \text{chronic disease}_2 + \ldots + \text{chronic disease}_{22} + \text{age} + \text{sex} + \text{region} \\ & + \text{care setting} + \text{Plan C}. \end{aligned} \quad (2)$$

We built the full model (equation (2)) in two steps to evaluate how the relationship between EHE mortality and chronic diseases changed before and after adjustment for an individual-level indicator of social vulnerability.

3. Results

3.1. Study subjects

There were 1649 deaths from all causes during the EHE in BC. We included 1597 decedents as cases in the study after excluding adults with missing information and children (figure 2). There were 2678 285 individuals in the pool of potential controls after exclusions, of which 7968 were included in the study following grouping and random selection (figure 2). Half of the subjects (50.0%) were assigned to the out-of-care group, and 27.1%, 20.3% and 2.6% were assigned to the residential care, hospital inpatient care, and ED care groups, respectively (table A.3). The study subjects (including cases and controls) were 47.6% female, and their ages ranged from 20 years to 114 years with a median of 78 years (table A.3). Consistent with the spatial distribution of the provincial population, most subjects (62%) resided in the greater Vancouver region [27]. Compared with controls, the cases had a higher proportion of individuals with chronic kidney disease, chronic obstructive pulmonary disease (COPD), heart failure, schizophrenia and substance use disorder (table 2). Most subjects (92.6% of cases; 91.0% of controls) had at least one pharmaceutical dispensed in the year before the EHE. More than twice as many cases (14.7%) as controls (6.3%) had at least one dispensation covered by Plan C indicating low-income status (table 2).

3.2. Chronic diseases

In the model without adjustment for individual-level low income (equation (1)), the ORs ranged from 0.74 [0.60, 0.89] for those included in the ischemic heart disease with angina registry to 2.43 [1.93, 3.06] for those included in the schizophrenia registry (figure 3). In the fully adjusted model (equation (2)), the OR for those with schizophrenia was 1.93 [1.51, 2.45]. Several other conditions were associated with higher odds of EHE mortality, including COPD (OR 1.48 [1.29, 1.71]), parkinsonism (OR 1.46 [1.03, 2.02]), heart failure (OR 1.45 [1.25, 1.68]), chronic kidney disease (OR 1.36 [1.18, 1.56]), ischemic stroke (OR 1.32 [1.05, 1.66]), and substance use disorder (OR 1.27 [1.07, 1.50]) (figure 3). Some conditions were associated with lower odds of EHE mortality, including osteoarthritis, depression, and ischemic heart disease with angina (figure 3). The ORs and 95% CIs for all other chronic diseases were not different from 1.0 (figure 3). The odds of EHE mortality were also higher with increasing multi-morbidity (see section A.1 in the supplementary appendix and figure A.1).

3.3. Social vulnerability

Compared with the ORs from the model that did not adjust for individual-level low income (equation (1)), adding the Plan C indicator (equation (2)) resulted in very little change for the ORs of most chronic diseases.

Table 2. Indicator of low-income and chronic diseases among the cases and controls.

Sample characteristic, n (%)	Cases ($N = 1597$)	Controls ($N = 7968$)
Covered by PharmaCare Plan C		
No	1245 (78.0%)	6749 (84.7%)
Yes	234 (14.7%)	504 (6.3%)
Unknown	118 (7.4%)	715 (9.0%)
Chronic disease presence		
Acute myocardial infarction	152 (9.5%)	636 (8.0%)
Alzheimer's disease and dementia	268 (16.8%)	1304 (16.4%)
Asthma	303 (19.0%)	1337 (16.8%)
Chronic kidney disease	439 (27.5%)	1619 (20.3%)
Chronic obstructive pulmonary disease	415 (26.0%)	1391 (17.5%)
Depression	752 (47.1%)	3651 (45.8%)
Diabetes	548 (34.3%)	2595 (32.6%)
Epilepsy	45 (2.8%)	176 (2.2%)
Gout	164 (10.3%)	746 (9.4%)
Heart failure	404 (25.3%)	1419 (17.8%)
Hospitalized transient ischemic attack	31 (1.9%)	162 (2.0%)
Hypertension	1120 (70.1%)	5525 (69.3%)
Ischemic heart disease with angina	200 (12.5%)	1120 (14.1%)
Ischemic heart disease without angina	341 (21.4%)	1406 (17.6%)
Ischemic stroke	111 (7.0%)	401 (5.0%)
Mood and anxiety disorders	109 (6.8%)	601 (7.5%)
Osteoarthritis	581 (36.4%)	3081 (38.7%)
Osteoporosis	307 (19.2%)	1573 (19.7%)
Parkinsonism	47 (2.9%)	182 (2.3%)
Rheumatoid arthritis	72 (4.5%)	356 (4.5%)
Schizophrenia	134 (8.4%)	300 (3.8%)
Substance use disorder	285 (17.8%)	969 (12.2%)

The exceptions were schizophrenia and substance use disorder, for which the OR was markedly reduced (figure 3). Compared with all other risk factors in the fully adjusted model, the Plan C low-income indicator had the highest OR at 2.42 [1.98, 2.95] (figure 3). Further adjustment for neighborhood deprivation scores from the CIMD did not affect the magnitude or precision of the estimates for individual-level low-income status or chronic diseases (figure A.2), and the ORs for the CIMD scores were null or had a marginal association with EHE mortality (see section A.2 in the supplementary appendix). The supplementary appendix includes ORs and 95% confidence intervals for all covariates in all models (table A.4).

4. Discussion

4.1. Summary

We compared differences in the prevalence of chronic diseases and social vulnerability between all adults who died during the 2021 EHE and similar adults who survived the event using a population-based case-control design. The risk factor most strongly associated with EHE mortality was receiving income assistance as identified using Plan C coverage for pharmaceutical prescription costs. The comorbidities most strongly associated with EHE mortality were schizophrenia, COPD, parkinsonism, heart failure, chronic kidney disease, ischemic stroke, and substance use disorder. Osteoarthritis, depression, and ischemic heart disease with angina were associated with lower odds of EHE mortality.

4.2. Comparison with our previous studies on the 2021 EHE in BC

In one of our previous case-only studies we compared all adults who died during the EHE with adults who died on the same dates in previous years [21]. We did not include indicators of social vulnerability in that study. When we compare the results from the case-only and case-control analyses, we find that schizophrenia is the comorbidity most strongly associated with EHE mortality in both studies. The OR in the case-only study was 3.07 [2.39, 3.94] and in the current study we reported 2.43 [1.93, 3.06] before adjusting for individual-level low income, and 1.93 [1.51, 2.45] after adjustment. We find identical results for chronic kidney disease with an OR of 1.36 [1.18, 1.56] in both studies, and similar results for ischemic stroke. The ORs for COPD, parkinsonism, and substance use disorder were elevated in the case-only study, and the ORs

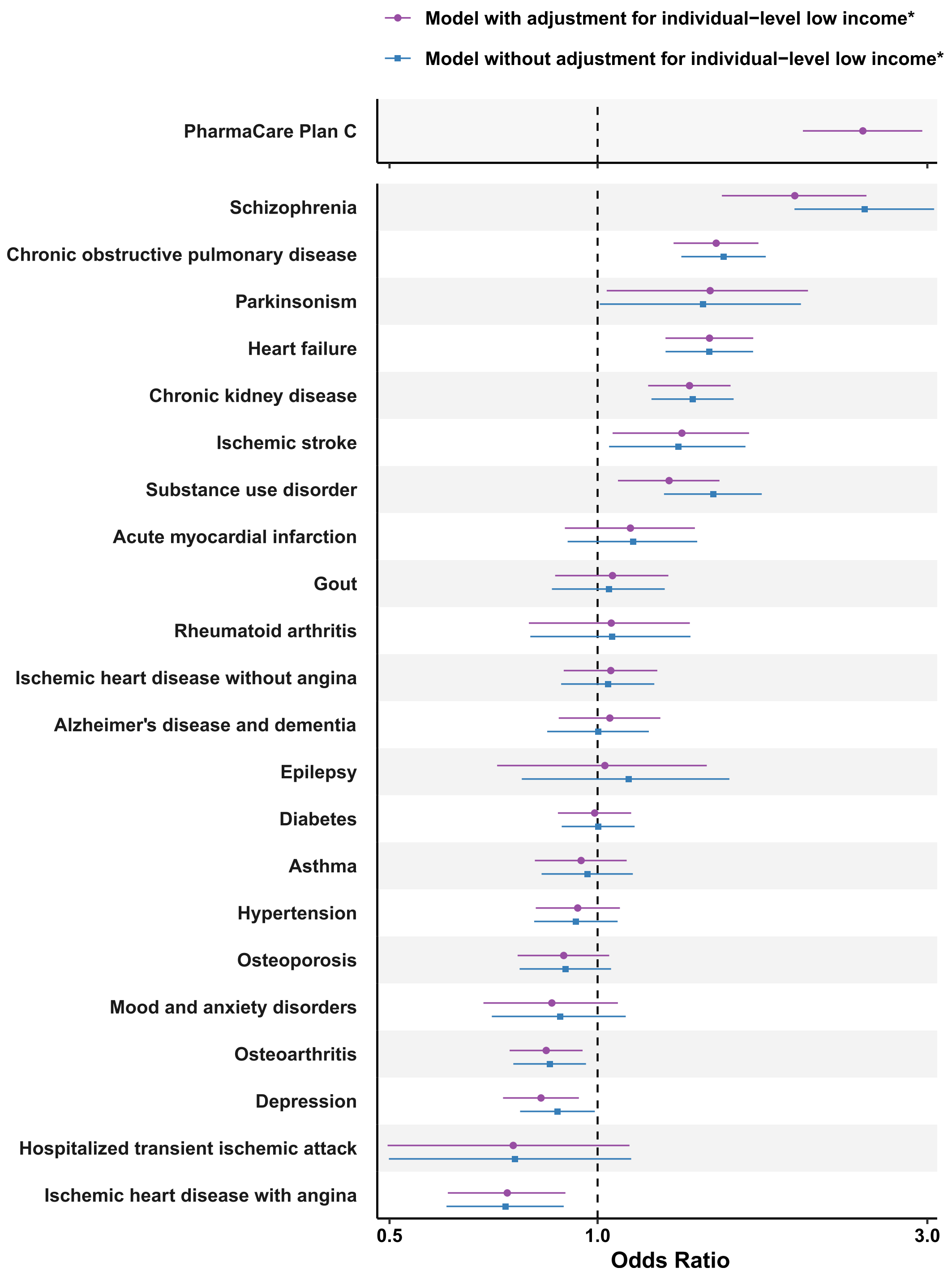

Figure 3. Chronic diseases, individual-level low income and mortality during the 2021 extreme heat event (EHE). Odds ratios and 95% confidence intervals are derived from logistic regression. The top panel shows the odds of PharmaCare Plan C coverage with no coverage as the reference category among EHE deaths (cases) compared with the controls. The bottom panel shows the odds of inclusion in the registry for each chronic disease among EHE deaths (cases) compared with the controls. The colors and shapes correspond to different models without (blue square, equation (1)) and with (purple circle, equation (2)) adjustment for individual-level low income. *Both models are adjusted for age category, sex, care setting, and health region of residence. Chronic diseases are ordered from top to bottom in each panel by the point estimates for the final fully adjusted model (equation (2)).

for these conditions in the case-control study were all higher than the ORs in the case-only study. The lowest OR in both studies was for ischemic heart disease with angina, which may indicate a protective effect of angina therapy.

We found that Alzheimer's disease and dementia were associated with lower odds of EHE mortality in the case-only study but found no difference between groups in this case-control analysis. Conversely, we found that heart failure was associated with higher odds of EHE mortality in this study but reported no difference between groups in the case-only analysis. These inconsistencies are likely due to the differences in study design. For example, heart failure is associated with a substantial risk of mortality regardless of weather conditions [39, 40]. It is possible that the higher odds of mortality associated with heart failure in this case-control study is not specific to the EHE. The same difference might be evident among any group of decedents and survivors selected from the BC population based on a specific time period, as done here. However, the difference may not be present when one group of decedents is compared with another group of decedents, because heart failure would have the same prevalence among those who died. Future analyses using a difference-in-differences design could address these limitations.

Our other previous case-only study compared community deaths (e.g. deaths that occurred in private residences or other community locations) during the 2021 EHE with community deaths during more typical weather at the same time of year from 2013 to 2020 [13]. The study was restricted to the greater Vancouver region, and it used an area-level combined index of social and material deprivation [13]. The adjusted OR in the case-only study was 2.88 [1.85, 4.49] for decedents living in the most deprived areas [13]. Here, we report a fully adjusted OR of 2.42 [1.98, 2.95] for the Plan C indicator of individual-level low income. Adding neighborhood deprivation scores from the CIMD to this model did not affect the magnitude or precision of any estimates (see section A.2 in the supplementary appendix and figure A.2). This suggests that, when available, individual-level variables are more useful than area-level variables for understanding heat risk.

4.3. Chronic diseases

4.3.1. Mental and behavioral disorders

Schizophrenia was the condition most strongly associated with EHE mortality (OR 1.93 [1.51, 2.45]). Adjusting for Plan C attenuated the overall ORs for schizophrenia (2.43 [1.93, 3.06] reduced to 1.93 [1.51, 2.45]) and substance use disorder (1.47 [1.25, 1.73] reduced to 1.27 [1.07, 1.50]), suggesting that some of the risk associated with these conditions can be attributed to social vulnerability. Some of the EHE deaths among those with substance use disorder may eventually be attributed to unregulated drug toxicity (an ongoing public health emergency in BC [41]), but the EHE likely compounded the mortality risk in this population. Studies conducted prior to the toxic drug crisis have reported associations between substance abuse and hot weather mortality and morbidity [42–45].

Other studies have reported similar results for mental and behavioral disorders [22, 46–48] and for schizophrenia specifically [10]. For example, a meta-analysis of case-control studies on heat wave-related deaths reported more than a 3-fold increase (OR 3.61 [1.3–9.8]) among those with psychiatric illness for both all-cause and heat-related deaths [22]. Similarly, a study in Adelaide, Australia found a 2-fold increase in deaths attributed to mental and behavioral disorders (incidence rate ratio (IRR) 2.40 [1.17–4.92]) and deaths attributed to schizophrenia-type disorders (IRR 2.08 [1.05–4.14]) during heat wave periods compared with non-heat wave periods [10].

There are multiple pathways linking mental and behavioral disorders to increased exposure vulnerability and susceptibility during extreme heat. First, schizophrenia and other mental illnesses may affect individual perception of the heat and the ability to respond appropriately to reduce exposure [48, 49]. Second, the physiological effects of heat exposure include impacts on the brain and its function [49], which could worsen symptoms of mental illness and the consequences of those symptoms. Third, several classes of pharmaceuticals used to treat mental and behavioral disorders are known to affect physiological thermoregulation, including antipsychotics, antidepressants, and anticholinergic drugs [49]. Fourth, severe mental health illness often co-occurs with substance use disorder. In addition to altering judgment and perception due to acute intoxication, some substances can also impair thermoregulation or hydration, in particular cocaine [43, 50] and alcohol [45]. Finally, schizophrenia, other mental illnesses and substance use disorders often coincide with social vulnerability [51], and a lack of social support and economic resources restricts the range of protective and adaptive behaviors available to people during EHEs.

4.3.2. Respiratory, cardiovascular, and cerebrovascular diseases

We report increased odds of EHE mortality associated with COPD, heart failure, and ischemic stroke. This is consistent with previous studies that have reported higher risk of heat wave-related mortality among those with respiratory [22], cardiovascular [22, 23], and cerebrovascular conditions [46]. In addition, review articles have found respiratory, cardiovascular, and cerebrovascular conditions to be primary causes of mortality and morbidity in the elderly during hot weather [24, 25]. Those with COPD may be more susceptible to effects from heat exposure because thermoregulation increases respiratory rates and volumes and because there are direct effects of hot air on the airways [52]. Air pollution during the EHE would also affect the ORs for COPD and other conditions. There was a prolonged air quality advisory in the greater Vancouver area due to high concentrations of ground-level O_3, and concentrations of $PM_{2.5}$ were also elevated [13, 21], both of which is common during EHEs [53]. Our case-control study design examines the association of the EHE period with mortality and was not designed to separate the effects of temperature and air pollution.

The cardiovascular system plays a key role in thermoregulation, placing those with reduced cardiovascular function at risk during hot weather [11]. The cerebrovascular system is also impacted because the changes in blood flow can affect the brain [11]. We observed higher odds of EHE mortality associated with heart failure and ischemic stroke, but not for other cardiovascular and cerebrovascular conditions. We observed no effect associated with previous acute myocardial infarction, ischemic heart disease without angina, or hypertension. We observed lower odds of EHE mortality associated with hospitalized transient ischemic attack and ischemic heart disease with angina. The differences between the existing literature and our results for cardiovascular and cerebrovascular conditions could be related to the overall decline in deaths from coronary heart disease observed in multiple countries globally since the 1980s [54]. Also, most heat-related deaths during the EHE occurred in private residences [31] and the most elderly and frail individuals with these conditions may have been protected in healthcare settings.

4.3.3. Chronic kidney disease

Renal disease is a well-recognized risk factor during hot weather, particularly chronic kidney disease [11]. Due to their role in maintaining fluid and electrolyte balance, the kidneys are involved in the thermoregulatory response to heat exposure and are also susceptible to injury when heat stress and/or dehydration cause a decrease in renal blood flow [11, 55]. Thus, EHEs likely pose a greater risk of injury to those with pre-existing chronic kidney disease and have also been linked to the development of the disease [56]. We report an OR of 1.36 [1.18, 56] associated with chronic kidney disease, consistent with Remigio *et al* [57] who found a 31% [1%, 70%] increase in the risk of same-day mortality during EHEs from 2017 to 2019 among patients with end-stage renal disease who were receiving hemodialysis treatment in three US cities. Similar results have been reported for renal morbidity in meta-analyses Lee *et al* [58] reported a 30% [20%, 40%] increase in kidney disease morbidity associated with high temperatures, and Bunker *et al* [24] reported a 2.12% [1.65%, 2.59%] increase in genitourinary morbidity in the elderly per 1 °C increase in ambient temperature.

4.3.4. Parkinsonism

We found an increased odds of EHE mortality associated with parkinsonism (OR 1.46 [1.03, 2.02]). Vandentorren *et al* [23] reported an OR of 3.52 [1.04, 11.98] for neurological disease associated with risk of non-accidental death in people aged 65 years and older during the 2003 EHE in France. Other studies of EHEs have reported elevated hospitalizations and deaths attributed to Parkinson's disease in Madrid, Spain [59], and excess hospital admissions in patients with underlying nervous system disorders in Chicago [60]. Parkinsonism can reduce mobility, awareness, and ability to care for oneself, which can all affect response to the heat [16, 60]. Also, Parkinson's disease is often treated with dopamine receptor agonists and anticholinergic drugs that affect thermoregulation by reducing thirst and impairing sweating, respectively [49].

4.4. Social vulnerability

Being covered by Plan C was the risk factor most strongly associated with EHE mortality in this study with an OR of 2.42 [1.98, 2.95]. Plan C covers all recipients of government administered income and disability assistance, meaning that it can identify low-income individuals if they filled a prescription at a community pharmacy in BC. We did not have access to a list of all plan recipients and could not classify the individuals who had not filled a prescription in the year prior to the EHE (<10% of subjects). In addition, Plan C cannot be used to identify all low-income individuals in the population because it only includes recipients of income and disability assistance. Monthly assistance rates vary by family size and individual factors (i.e. disabled versus employable) [61], but none exceed the cost of a basic standard of living in any region of BC as determined by Statistics Canada [62].

When it comes to heat-related mortality, individual-level measures of social vulnerability are studied much less frequently than the more widely available area-level measures. Furthermore, individual-level measures of education, occupation or ethnic group are more commonly used than income. For example, Benmarhnia *et al* [63] reported a pooled relative risk of 1.03 [1.01, 1.05] for low individual socio-economic status associated with high ambient temperatures from a meta-analysis of 15 studies. However, only one of the 15 studies measured individual-level income. Specifically, a study of high temperatures and mortality in Seoul, Korea from 2000–2002 found that the excess mortality rate was 4.7% [−1.5%, 11.4%] among low-income individuals compared with 2.7% [0.5%, 5.1%] among the general population, when temperatures exceeded 30.5 °C [64]. A more recent study in the Netherlands during 2006, 2018 and 2019 linked death records to household income from tax registries [65]. It reported a 2.60% [2.27%, 2.93%]

higher mortality rate among the lowest income group compared with a 0.77% [0.32%, 0.92%] higher mortality rate among the highest income group for every 1 °C increase in temperature above 16 °C [65].

4.5. Limitations

The secondary use of administrative health data in this study has important limitations. Administrative health data are not collected for research purposes, and they cannot be used to directly assess many of the risk and protective factors that affect the relationship between extreme heat and mortality, such as housing characteristics or use of air conditioning [11, 16]. For some individuals, administrative health data may be missing for reasons that are not clear. For example, when a residential location is missing in the client roster, it could be because the individual lives outside of BC or the individual may be unhoused. By excluding cases and potential controls that had missing residential location in the client roster, some unhoused people living in BC may have been excluded from the study. We expect the impact of this limitation to be minor because the Coroners Service reported that only 3 of the 619 heat-related deaths (0.5%) that occurred during summer of 2021 in BC were experiencing homelessness [31].

In addition, some of the relevant administrative health data were either incomplete or unavailable due to delays, access restrictions, or health system irregularities. For example, data completion was delayed for the Health System Matrix (complete for the 2018–2019 fiscal year, which runs from April to March) and the chronic disease registries (complete to 31 March 2020). Similarly, data on ED visits were incomplete because some small hospitals in BC do not contribute data to NACRS. As described above, Plan C is not a perfect indicator of individual-level low-income status. Further, we did not have information on length of residency in BC, which could affect inclusion in the Health System Matrix and the chronic disease registries. The impacts of these data limitations are likely similar between the case and control groups. Finally, the ORs from the models in this study describe correlations and are not meant to be interpreted as unbiased causal effect estimates.

4.6. Conclusion and future directions

Our study strengthens the evidence base on the mortality impacts of EHEs in several ways. We used a population-based case-control design and linked administrative health data to study the mortality impacts of an unprecedented EHE that occurred recently in a temperate region. In addition, we used an individual-level indicator of social vulnerability along with chronic diseases to identify risk factors for death during the EHE. We found that individual-level low income and schizophrenia were most strongly associated with mortality during the 2021 EHE in BC. Other risk factors for mortality were COPD, parkinsonism, heart failure, chronic kidney disease, ischemic stroke, and substance use disorder. Our future work will build on this initial case-control study to examine other potential risk factors such as dispensed pharmaceuticals. We will also use the same data platform to further investigate schizophrenia and morbidity outcomes.

Along with our previous case-only studies on this EHE [13, 21] and information on the heat-related deaths reported by the Coroners Service [31], the findings from this study are being used to inform public health policy and practice in BC. For example, since the 2021 EHE, BC has implemented a province-wide Heat Alert and Response System that details the criteria used to issue a Heat Warning or an Extreme Heat Emergency, the appropriate public health messaging for both types of alerts, and the recommended actions for health sector and other partners [66]. Planning ahead to conduct health checks and to move susceptible individuals from dangerously hot to cooler environments is recommended for multiple groups and agencies [66]. BC has also implemented a program to provide free portable air conditioning units to low-income individuals and households [67]. Beyond emergency response, longer-term interventions must focus on adaptations to prevent EHE deaths, such as retrofitting older buildings with mechanical cooling as needed, promoting building designs that incorporate passive cooling measures, and increasing tree canopy cover in urban areas.

Data availability statement

Access to data provided by the Data Stewards is subject to approval but can be requested for research projects through the Data Stewards or their designated service providers. For detailed information on how to request access to this data see Government of British Columbia [68].

The data that support the findings of this study are available upon reasonable request from the Data Stewards.

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Author contributions

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Conflict of interest

The authors declare they have no conflicts of interest related to this work to disclose.

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