

Proceeding Paper

# Heat Waves and Cardiovascular Events in Milan, Italy: A Geospatial Case-Crossover Approach Using Data from Emergency Medical Services <sup>†</sup>

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**Abstract:** Heat waves (HWs) are becoming more frequent due to climate change. Their impact on cardiovascular (CV) health has been widely studied, and results vary depending on the disease and the geographic area. Our aim was to study this phenomenon using emergency medical service (EMS) data relevant to CV events that occurred out-of-hospital during May–Sept in 2020 and 2021 in Milan, Italy. Mean daily temperature (MDT) was computed in the city, and normal (NL), HW, or extreme HW were defined as days with MDT <90th, ≥90th, and ≥98th percentiles, respectively, resulting in 232 NL and 74 HW days, of which 16 were extreme. In total, 20,266 CV events were reported by EMS (53% in women, 55% in ≥65 yo). A case-crossover design was applied to calculate the odds ratio of the events in HW and extreme HW compared to NL days, accounting for diagnosis and geolocation. Increased odds were found for acute myocardial infarction (1.53 and 1.56), congestive heart failure (2.47 and 2.81), and intermediate coronary syndrome (2.08 and 6.11). Our study showed the potential of using EMS for analyzing the effects of HW on CV health, thus the confirming negative impact of rising temperature.

**Keywords:** heat; cardiovascular health; case-crossover design



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## 1. Introduction

As a result of climate change, recognized as the greatest health threat of the 21st century [1], extreme heat days are becoming more frequent, resulting, in 2018, in an additional 220 million heat wave exposure events in the whole world compared to the average in the 1986–2005 period [2]. In addition, it was estimated that over 70,000 deaths were due to the 2003 European heat wave which particularly severely hit Italy, France, and Spain [2,3]. The relationship between temperature and cardiovascular (CV) diseases has been hypothesized as U-shaped, with both lower and higher temperatures contributing to the increase in their occurrences [1,2,4–6]. The increase in mortality noted during extremely high temperature was mainly caused by the increase in mortality due to CV and cerebrovascular diseases [4,7].

From a biological standpoint, due to the pathophysiological implications of heat exposure, the influence of high temperatures on human health is plausible [2,4,8]. The impact of temperature on CV morbidity and mortality has been widely studied in the literature, especially in recent years [2,6]. While previous results are consistent with increased mortality at higher temperatures, their impact on morbidity is more complex. Many studies showed a small or no increase in CV morbidity during heat, and the tendency also varied depending on the type of disease [6,9,10].

Most of these studies examined whole cities or even broader geographic areas. Due to the differences in population heat sensitivity and urban heat stress, the results from one geographic area may not be applicable to another [7]. Moreover, only several studies accounted for the effect of an urban heat island (UHI) within a city, the health-related consequences of which are inconclusive [1,11].

In this study, our aim was to retrospectively study the effects of heat waves (HWs) and extreme HWs on emergency CV events in Milan, Italy, using geolocalized emergency out-of-hospital medical service (EMS) data and applying a case-crossover design, accounting for gender and age, as well as geolocation of the event and the medical diagnosis, to calculate the odds ratio (OR) of such events compared to days with normal (NL) temperature.

## 2. Methodology

Milan is the capital of the Lombardy region in northern Italy. In 2020, its population was equal to almost 1.4 million people, of whom over 300,000 were older than 65 years [12]. According to the Köppen–Geiger climate classification, the city is located in the Cfa zone, meaning it has a humid subtropical climate characterized by hot summers and no dry season [13]. There are no significant differences in elevation in the city. Milan is divided into 88 nuclei of local identity (in Italian: Nuclei di Identità Locale; NIL), which form zones of diverse socio-demographic characteristics.

### 2.1. Data

The source of meteorological data was the Regional Agency for Environmental Protection (in Italian: Agenzia regionale per la protezione dell'ambiente; ARPA) for the Lombardy region, established in 1999. The institution provides open data from its measurement stations relevant to various meteorological parameters, which can be downloaded from the website [14]. For the purpose of this study, based on the Voronoi diagram [15], all the temperature stations allowing coverage of the whole city territory were selected. This resulted in the gathering of hourly data for temperature at 2 m above the surface for 2020 and 2021 from 9 stations located within Milan and its surroundings. From these stations, the mean daily temperature was calculated as the average of records, and with arbitrarily defined thresholds, it was used to characterize a HW (i.e., days with mean daily temperature greater than or equal to the 90th percentile of the yearly temperature distribution) or an extreme HW (i.e., mean daily temperature greater than or equal to the 98th percentile).

Data relevant to the EMS within the Lombardy region for years 2020 and 2021 were provided upon request by the Regional Agency for Emergency and Urgency (in Italian: Agenzia Regionale Emergenza Urgenza; AREU). They included information about the events that were internally classified as CV once reported through the emergency numbers 112 (European) or 118 (national). For each event, the available data included the gender and age of the patient, its approximate location relevant to the place of call (e.g., latitude and longitude), time (e.g., year, month, day, and hour of the event), and basic medical information (e.g., general reason for the report). For this study, only the events that took place in Milan were selected.

A complementary source of data was represented by Emergency Urgency On Line (in Italian: Emergenza Urgenza On Line; EUOL), which is a system providing hospital data for the Lombardy region. These data included, among others, hospital, triage, and medical details, and were used to add the official diagnosis once the patient was admitted to the emergency room in the hospital, expressed in the International Classification of Diseases codes—ICD-9 [16], to the AREU records. Also, fatal events could be identified based on EUOL data.

To conduct a disease-specific analysis, the cumulative number of cases for each disease based on ICD-9 was computed; then, only those that accounted for at least 1% of all identified cases were considered, and within such diagnoses, only those relevant CV conditions were selected for further processing.

As the focus of this study was to analyze the effect of high temperatures, only events in the summer period, from May to September, were included. It must be noted that August is a holiday period in Italy. In order to account for the vacation effect, the daily number of CV events was standardized according to mean traffic data retrieved from the Open Data portal of the Lombardy Region [17]. This database provides the number of vehicles transiting on selected roads in Milan each day, which can be used as a proxy estimate of the presence of the inhabitants of the city. For this purpose, the daily number of CV events was divided by the difference between the mean traffic on the corresponding day and the yearly mean traffic on all available streets.

### 2.2. Statistical Methods

First, a descriptive analysis relevant to the weather variables and EMS data was applied. It included the examination of the mean, minimum, and maximum values of hourly or daily temperature in the analyzed period. EMS data were stratified by patient-related (i.e., gender, age) and event-related (i.e., place, time, diagnosis) factors. Second, the OR was analyzed, applying the case-crossover design [18]. The odds analysis is a measure of effect size in logistic regression modelling [18]. The case-crossover design was first formulated by Maclure (1991) [19] as a method for studying transient effects on the risk of acute events. The method is a combination of case-control study [20], widely used in epidemiology, and the crossover design, which allows the limitation of the between-person confounding factor of the former method to be overcome by using each subject as its own control [19,21]. For the purpose of our study, a time-stratified case-crossover design was applied, and the exposure factors were HW and extreme HW. The results were used as an input to the geospatial analysis, the purpose of which was to identify the NIL most vulnerable to heat. Odds ratios and their confidence intervals were estimated using the Cochran–Mantel–Haenszel method [21]. Short windows from 1 to 7 days before the heat event were tested in order to assess the sensitivity of the OR analysis.

Data were pre-processed and analyzed by software using Python (version 3.8.5); the geospatial part was performed in QGIS (version 3.16 Hannover). Descriptive statistics are provided in absolute numbers, while standardized values are used in OR analysis.

### 3. Results

The mean daily temperature for summer periods was equal to 22.7 °C, with a minimum of 12.9 °C and a maximum of 30.5 °C. The maximum hourly temperatures registered in Milan were 37.7 °C and 37.3 °C for 2020 and 2021, respectively. The 90th percentile of mean daily temperature was equal to 25.8 °C and 25.7 °C, for 2020 and 2021 respectively, while the 98th percentile was 28.0 °C for both years. Based on these values, for each year, there were 37 HW days, of which 8 were of extreme HW, with all happening between June and August. The summary of descriptive statistics for the temperature is presented in Table 1.

**Table 1.** Descriptive statistics of summer (May–September) temperature in Milan for 2020 and 2021.

	Non-Heat Days	Heat Wave (Incl. Extreme Heat Wave) Days	Extreme Heat Wave Days
Count	21.3 °C	27.1 °C	28.9 °C
Mean	3.06 °C	1.15 °C	0.84 °C
Standard deviation	12.9 °C	25.7 °C	28.0 °C
Minimum	19.2 °C	26.3 °C	28.3 °C
25%	21.8 °C	26.8 °C	28.4 °C
50%	23.7 °C	27.9 °C	29.7 °C
75%	25.8 °C	30.5 °C	30.5 °C
Maximum	21.3 °C	27.1 °C	28.9 °C

In 2020 and 2021, during the summer months, 20,266 CV events were reported via the emergency telephone number. In general, more females than males and more elderly people (above 65 years old) than young people were subjected to an out-of-hospital event.

A significant change in proportions was observed in stratification by age and place during HW or extreme HW compared to days with NL temperatures. A greater percentage of young people compared to elderly people were subject to a CV event during HW (47% vs. 45%, respectively). Moreover, during both HW and extreme HW, a smaller fraction of events occurred at home (70% and 69%, respectively), while an increase in the proportion of events happening outside on the street, as well as in other places (e.g., a public office, sports facility, or workplace), was noticed.

No significant differences in the distribution of events occurring at night or during the day were found. The summary of descriptive statistics for CV events that happened during the summer period for the two years considered in the analysis is presented in Table 2. Significant results at an alpha level of 5% are marked with an asterisk. The merging process with EUOL data in order to add the diagnosis and mortality to EMS data was possible only in 63% (12,768 patients) of the total cases.

**Table 2.** Descriptive statistics of CV events in Milan during summer (May–September) 2020 and 2021.

	Non-Heat Days	Heat Wave (Incl. Extreme Heat) Days	Extreme Heat Wave Days	Total
Gender				
Female	8305 (54%)	2525 (53%)	488 (53%)	10,830 (53%)
Male	7199 (46%)	2237 (47%)	436 (47%)	9436 (47%)
Age				
<65	6997 (45%)	2222 (47%) *	438 (47%)	9219 (45%)
>=65	8507 (55%)	2540 (53%) *	486 (53%)	11,047 (55%)
Place				
Home	11,583 (75%)	3353 (70%) *	639 (69%) *	14,936 (74%)
Street	1286 (8%)	479 (10%) *	102 (11%) *	1765 (9%)
Other	2635 (17%)	930 (20%) *	183 (20%) *	3565 (18%)
Hour				
Night (00-08)	3385 (22%)	1051 (22%)	192 (21%)	4436 (22%)
Day (09-23)	12,119 (78%)	3711 (78%)	732 (79%)	15,830 (78%)
Total	15,504	4762	924	20,266

\*:  $p < 0.05$  vs. non-heat days (Fisher’s Z-Test).

The applied diagnosis selection criteria resulted in the definition of eight diseases: acute myocardial infarction (ICD-9 code: 41090), atrial fibrillation (42731), cardiac arrest (4275), congestive heart failure (4280), hypertension (4011 or 4019 or 99791), intermediate coronary syndrome (4111), palpitations (7851), and tachycardia (4270 or 7850).

In total, there were 1751 cases relevant to the aforementioned CV diseases; the most frequent diagnosis was hypertension, representing 30% of all cases, followed by atrial fibrillation (18%), palpitations (12%), tachycardia (11%), congestive heart failure (10%), cardiac arrest (9%), intermediate coronary syndrome (5%), and acute myocardial infarction (4%). Among them, only cardiac arrest was characterized by a high mortality rate (68% of the cases), followed by acute myocardial infarction with a mortality rate of less than 3%. For cardiac arrest, compared to non-heat days, the fraction of fatal events that occurred during HW was higher by more than five percentage points and by more than eight percentage points for those that happened during extreme HW. The summary of descriptive statistics for each specific CV disease is presented in Table 3.

**Table 3.** Descriptive statistics for each specific CV disease as cause of admission to the emergency room during summer 2020 and 2021 in Milan, considering the 63% of EMS data for which it was possible to retrieve the diagnosis.

	Non-Heat Days	Heat Wave (Incl. Extreme Heat) Days	Extreme Heat Wave Days	Total
Acute myocardial infarction				
Events	55	21	5	76
In which fatal events	0 (0.0%)	2 (9.5%)	2 (40.0%)	2 (2.6%)
Atrial fibrillation				
Events	251	66	17	317
In which fatal events	1 (0.4%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
Cardiac arrest				
Events	118	36	4	154
In which fatal events	79 (66.9%)	26 (72.2%)	3 (75%)	105 (68.2%)
Other	2635 (17%)	930 (20%)*	183 (20%)*	3565 (18%)
Congestive heart failure				
Night (00-08)	3385 (22%)	1051 (22%)	192 (21%)	4436 (22%)
Day (09-23)	12,119 (78%)	3711 (78%)	732 (79%)	15,830 (78%)
Total	15,504	4762	924	20,266
Hypertension				
Events	456	78	13	534
In which fatal events	0 (0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Intermediate coronary syndrome				
Events	71	16	5	87
In which fatal events	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Palpitations				
Events	172	39	6	211
In which fatal events	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Tachycardia				
Events	156	40	5	196
In which fatal events	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Total				
Events	1416	335	63	1751
In which fatal events	81 (5.7%)	30 (9.0%)	5 (7.9%)	111 (6.3)

\*:  $p < 0.05$  vs. non-heat days (Fisher's Z-Test).

The OR analysis using case-crossover design was first applied to the AREU data only, standardized by traffic, to answer the question of whether HW and extreme HW increase the odds of having an emergency CV event. As a second step, it was applied to the merged AREU and EUOL data to answer the same question for each specific CV condition.

A time window of 3 days brought the most significant results, but all of the tested windows (1–7 days) produced similar outcomes, with a significant all-cause OR of 1.07 (95% CI: [1.00; 1.14]) for HW (Table 4). The heat effect, which was not statistically significant, was found to be stronger for males than females (+8% against +6% of odds in HW and +12% against –1% in extreme HW). In populations older than 65 years, an increase (+6%) in odds in HW was found; however, it was also not significant.

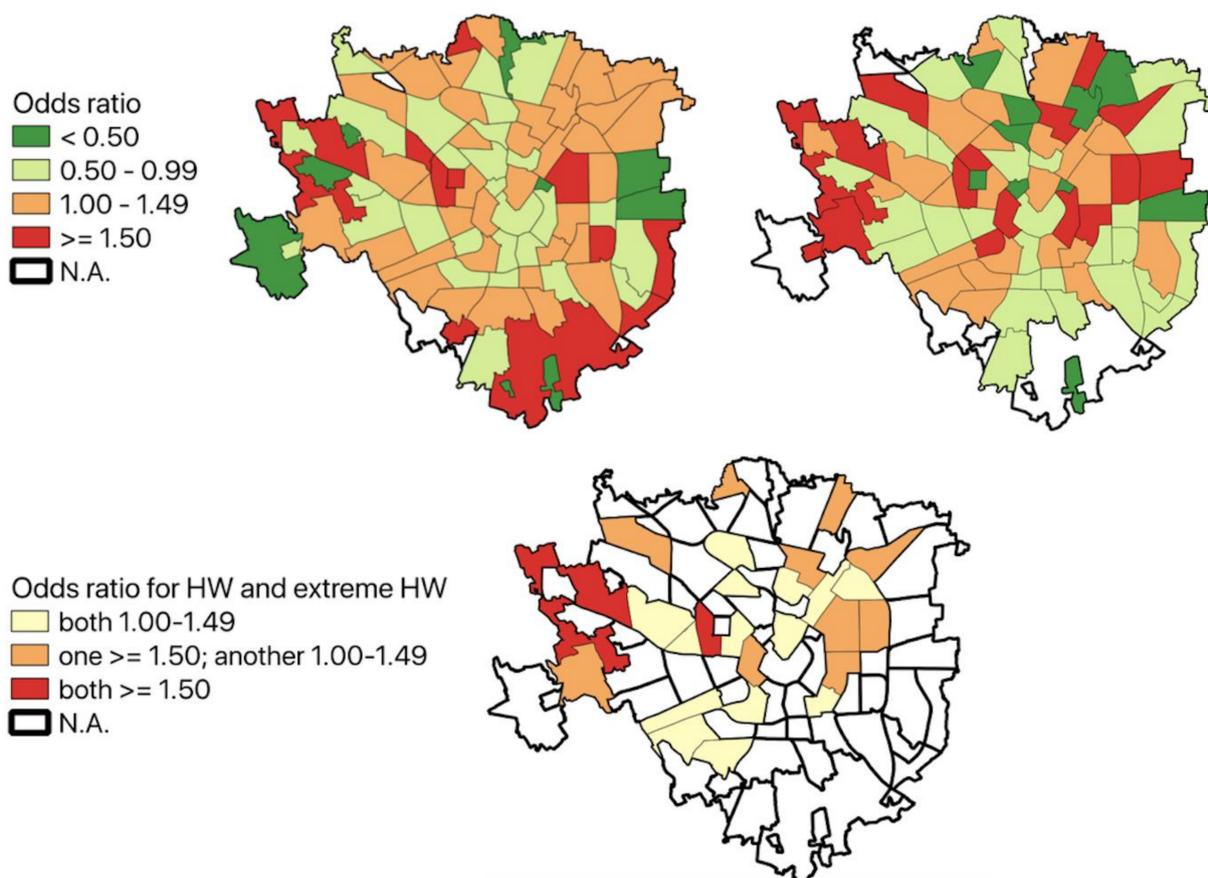
The ORs calculated for each of the 8 diagnoses of CV diseases notably vary in effect and strength. In particular, significantly increased odds for HW were found for congestive heart failure (2.47), while only a trend of increase was noticed for acute myocardial infarction (1.53 ( $p = 0.45$ ) and 1.56 ( $p = 0.65$ ), respectively), and intermediate coronary syndrome (2.08 ( $p = 0.26$ ) and 6.11 ( $p = 0.15$ ). Interestingly, the condition of extreme HW compared to HW led to a change, hence not significant, from a negative to a positive odds ratio for atrial fibrillation (from 0.98 to 1.42) and palpitations (from 0.73 to 1.88). The probability of occurrence of resulting cardiac arrest, hypertension, and tachycardia was not affected.

**Table 4.** Odds ratio with 95% confidence intervals for each CV disease, considering a time window of 3 days.

	Non-Heat Days	Heat Wave (Incl. Extreme Heat) Days	Extreme Heat Wave Days	Total
All patients	1.07 *	[1.00; 1.14]	1.05	[0.90; 1.23]
≥65 years old	1.06	[0.97; 1.16]	0.95	[0.77; 1.18]
Female	1.06	[0.97; 1.16]	0.99	[0.80; 1.22]
Male	1.08	[0.98; 1.189]	1.12	[0.87; 1.43]
Acute myocardial infarction	1.53	[0.52; 4.5]	1.56	[0.24; 10.04]
Atrial fibrillation	0.98	[0.57; 1.69]	1.42	[0.4; 5.07]
Cardiac arrest	0.99	[0.49; 2.01]	0.47	[0.09; 2.57]
Congestive heart failure	2.47 *	[1.09; 5.62]	2.81	N.A.
Hypertension	0.74	[0.46; 1.19]	0.70	[0.23; 2.14]
Intermediate coronary syndrome	2.08	[0.59; 7.34]	6.11	[0.51; 72.66]
Palpitations	0.73	[0.37; 1.45]	1.88	[0.16; 21.5]
Tachycardia	0.87	[0.43; 1.74]	0.29	[0.03; 2.49]

\*:  $p < 0.05$  vs. non-heat days (Fisher’s Z-Test). N.A.: not available

As a last step, a spatial analysis calculating the OR for all-cause CV events in each NIL within the city of Milan (Figure 1) was performed. Several neighborhoods appear to have a higher OR relevant to HW, and for some of them, this OR is maintained or, for extreme HW, even increased.



**Figure 1.** Top panels: OR of the occurrence of CV event computed within a time window of 3 days for each NIL in Milan, during HW (left) and extreme HW (right). Bottom panel: the NIL in which OR was  $\geq 1$  for both HW and extreme HW are highlighted.

#### 4. Discussion

In extremely high temperatures, the human thermoregulation system may not generate appropriate responses to thermal stresses, causing an increase in the risk of morbidity and mortality [6]. Our outcomes confirmed the negative impact of high temperatures on CV health. The most significant results were obtained using a time window of 3 days, which is in line with previous studies, which reported that the effects of heat waves on health appear rapidly and last for a short time [1,5,7,22]. Most of the studies examining the relationship between temperature and CV health analyzed changes in hospital admissions, odds ratios, or relative risks, estimated through distributed lag linear or non-linear models. When the effect of a factor is not very strong, the odds ratio provides an approximation of the relative risk [23]. Compared to previous studies, we focused our analysis on data from the EMS, relevant to calls to the emergency telephone number during the summer period with relevance to CV diseases, which were further confirmed and specified in eight different causes using data relevant to the following hospital admission to the emergency room.

It is not evident whether high temperatures increase all-cause CV hospitalization [24–27]. The decrease in OR of hospitalization due to hypertension we found in Milan is in agreement with previous studies by Bauer et al. (2022) [28], Lin et al. (2009) [25], and Schulte et al. (2021) [10], which reported a decrease in the number or risk of hospital admissions. Conversely, we found a positive OR for congestive heart failure, which was also estimated by Koken et al. (2003) [29] and by Qiu et al. (2013) [30].

The strength of high temperature effects on acute coronary syndrome was significantly different in two Chinese cities; the risk of hospitalization increased by 3.4% in Beijing [31] and by as much as 66% in Yancheng [32]. In Milan, we found a particularly high OR for intermediate coronary syndrome for both heat waves and extreme heat waves. Nevertheless, a negative association between mean temperature and hospital admissions for acute coronary syndromes was found in Athens [33].

The higher odds of hospitalization due to acute myocardial infarction with heat waves that we found for Milan were also reported in Finland [34], Iran [35], and the United States [27,36]. Moreover, two studies from Australia and South Korea attributed the higher risk to particular socio-economic groups [37,38]. On the contrary, studies in China [39], Denmark [40], France [41], and Spain [42] found no or a decreasing relationship between heat and myocardial infarction or ST-segment elevation myocardial infarction. In addition, a study in Vietnam revealed an opposite influence in two parts of the same country [43].

No influence on hospitalization due to heat was reported for arrhythmia, or specifically, for atrial fibrillation, in Canada [44] and the United States [45]. However, an Italian study reported a slight negative correlation between temperature and acute onset of atrial fibrillation [46]; a decrease in arrhythmia hospitalization with heat was also found in Finland [34], while the relationship in South Korea varied by city [47]. Our study reported no significant influence of HW on atrial fibrillation hospital admissions, and a decrease in odds for palpitations, while extreme HW conditions increased the odds of hospitalization in both conditions.

It was previously found that the risk of out-of-hospital cardiac arrest with heat was higher compared to that for non-heat in Korea [9] and Japan [48]. A study examining the effects of the 2003 heat wave in Paris [41] reported a particularly strong relationship, but only for people over 60 years old. Our results, which revealed a decrease in OR for cardiac arrest, are apparently in contrast with those studies and in agreement with [49], which found a reduced number of out-of-hospital cardiac arrests with heat in Iran.

It was pointed out that the impact of temperature extremes on CV diseases is difficult to assess as the temperature–morbidity and –mortality associations vary due to several factors, including age, race, and gender [1,4,22]. A negative impact of heat was reported to be stronger for females than males in suburban areas [1] or regardless of area [11]. Also, previous results showed an increase in elderly morbidity and mortality with high temperatures [1,5,7,9,22]. Our results relevant to CV emergency events (including both

fatal and non-fatal) for the city of Milan go in the opposite direction, showing a higher impact on males and the younger population.

Humans' sensitivity to heat also depends on socio-economic and urban factors, such as income, access to education, health care facilities, and air conditioning [1]. A greater risk of CV mortality has been attributed to illiterate people as well as to areas with a lower number of hospital beds per 1000 inhabitants [1]. Using a scale classifying Beijing into zones of just four levels of urbanization (high, medium-high, medium, and low), Xing et al. (2020) [1] found that more highly urbanized areas had significantly lower temperature–CV mortality risks than lesser urbanized zones. On the contrary, a study conducted in London using small geographic partitions of approximately 2000 inhabitants (lower-layer super output areas) found no spatial pattern in all-cause mortality odds [11]. Further, Murage et al. (2020) [11] found a positive influence of vegetation cover on the reduction of the number of deaths in London, while no such relationship was found for socio-economic factors. Many other studies have particularly highlighted the role of city vegetation and identified its increase as one of the most effective solutions for city heat vulnerability mitigation [50–52]. In addition, it was argued that the building characteristics have a greater influence on the indoor temperature than does the geolocation itself [11]. In general, the spatial relationship (including the aspect of the UHI) between CV events is not consistent and varies depending on geographic area [1].

The above-mentioned factors may explain the lack of pattern in the geospatial OR analysis of CV events in Milan. Moreover, division into 88 zones may be too narrow of a partition, considering the number of events recorded in the two summer periods analyzed in this study. An extension of the analysis to additional years and the aggregation of NIL based on urbanistic criteria, for example, heat vulnerability, might help in finding unequivocal conclusions about specific increased risks in a certain area of the city compared to others.

Although heat-related health vulnerability has decreased in recent decades as the population has adapted to extreme temperatures [3,53,54], the impact of heat waves on CV morbidity and mortality is still significantly negative, and there is a strong need for mitigation strategies [8]. Some authors argue that during particularly high temperatures, people die before being transported to the hospital more often than during non-extreme meteorological conditions [4,9,10]. In this perspective, one strength of our study is that we performed the analysis for cases reported via the emergency telephone number, regardless of whether a patient was dead or alive at the arrival of an ambulance. The main limitation of our study is that a period of only two summers, to some extent also influenced by the pandemic, was studied. In addition, we considered heat days as separate points in time and did not analyze the cumulative duration of the wave, which can produce different conclusions [5]. In addition, we did not adjust our results by considering other weather and air-quality indicators.

The inconsistency of previous results regarding CV disease-specific morbidity and mortality proved the importance of conducting deeper studies in this area. Further research focusing on the city of Milan should also account for the perceived temperature as well as consider a new neighborhood aggregation in order to find the geospatial health-related dependencies related to specific characteristics of the territory and its resident population.

## 5. Conclusions

This study provided a description of CV health effects due to heat wave events in the city of Milan during the summers of 2020 and 2021. Our study showed the potential for using EMS data, in conjunction with the official diagnosis of CV disease at patient admission to the hospital, to analyze the effects of heat wave events on CV health. The cases reported via emergency telephone numbers were stratified by patient-related, event-related, and medical-related factors, and odds ratio analysis in case-crossover design, including geospatial analysis, was performed. The presented results confirmed the negative impact of high temperatures on CV health, with increased odds of occurrence for acute myocardial

infarction, congestive heart failure, and intermediate coronary syndrome. Further research is needed to fully comprehend these phenomena and their causes in order to develop mitigation actions to improve resilience in the resident population.

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**Conflicts of Interest:** The authors declare no conflict of interest.

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