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Temperature-mortality association during and before the COVID-19 pandemic in Italy: A nationwide time-stratified case-crossover study

Wenhua Yu a, Rongbin Xu a, Tingting Ye a, Chunlei Han b, Zhuying Chen c, Jiangning Song d, Shanshan Li a,*, Yuming Guo a,*

a Climate, Air Quality Research Unit, School of Public Health and Preventive Medicine, Monash University, Level 2, 553 St Kilda Road, Melbourne, VIC 3004, Australia
b School of Public Health and Management, Binzhou Medical University, 346 Guanhai Road, Yantai 264003, PR China
c Department of Biomedical Engineering, The University of Melbourne, 203 Bouverie Street, Melbourne, VIC 3053, Australia
d Monash Biomedicine Discovery Institute, Department of Biochemistry and Molecular Biology, Monash University, Melbourne, VIC 3800, Australia

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ABSTRACT

Objectives: To identify the associations of temperature with non-COVID-19 mortality and all-cause mortality in the pandemic 2020 in comparison with the non-COVID-19 period in Italy.

Methods: The data on 3,189,790 all-cause deaths (including 3,134,137 non-COVID-19 deaths) and meteorological conditions in 107 Italian provinces between February 1st and November 30th in each year of 2015–2020 were collected. We employed a time-stratified case-crossover study design combined with the distributed lag non-linear model to investigate the relationships of temperature with all-cause and non-COVID-19 mortality in the pandemic and non-pandemic periods.

Results: Cold temperature exposure contributed higher risks for both all-cause and non-COVID-19 mortality in the pandemic period in 2020 than in 2015–2019. However, no different change was found for the impacts of heat. The relative risk (RR) of non-COVID-19 deaths and all-cause mortality at extremely cold (2 °C) in comparison with the estimated minimum mortality temperature (19 °C) in 2020 were 1.63 (95% CI: 1.55–1.72) and 1.45 (95% CI: 1.31–1.61) respectively, which were higher than all-cause mortality risk in 2015–2019 with RR of 1.19 (95% CI: 1.17–1.21).

Conclusion: Cold exposure indicated stronger impacts than high temperatures on all-cause and non-COVID-19 mortality in the pandemic year 2020 compared to its counterpart period in 2015–2019 in Italy.

1. Introduction

The coronavirus disease 2019 (COVID-19) has caused a devastating socioeconomic disruption as well as an unprecedented challenge to public health. Most governments have imposed dramatic restrictive containment measures such as quarantines and lockdown, border and travel restrictions, and resource reorganization to limit viral diffusion and reduce deaths from infection. However, those
restricted activities also, directly and indirectly, cause profound impacts on people’s lives and health. For example, stay-at-home orders would directly decrease outdoor physical activities and change the pattern of social contacts (Prem et al., 2020; Wang et al., 2020). It may also indirectly lead to the damage of health through delayed health care for acute emergencies (De Filippo et al., 2020; De Rosa et al., 2020), exacerbations of chronic diseases (Wang and Zhang, 2020), and psychological depression (Weinberger et al., 2020). Therefore, whether the individual vulnerability to the temperature-mortality association would be affected by the pandemic remains elusive.

The temperature-mortality relationship in different climates and populations may exhibit significant variation (Carder et al., 2005; Gasparrini et al., 2015b). Generally, the non-linear temperature-mortality association is mainly described as a J-, V-, or U-shaped curve in different regions and countries (Gasparrini et al., 2015b; Guo et al., 2013; Guo et al., 2014; Ryti et al., 2016). The association could be affected by many factors like geographic locations, climatological and socioeconomic conditions, human behaviours (Gasparrini et al., 2015b), and social interventions (Liotta et al., 2018). For example, a quasi-experimental study conducted in Italy implied that a community connection intervention program to reduce social isolation and improve the individual social network prevented heat-related mortality in the elderly (Liotta et al., 2018). Therefore, it is warranted to identify the possible change of the temperature-mortality association in the pandemic period when people's lives, socio-economic activities, and health care quality have been hugely altered due to the restrictive social interventions and individual responses to the pandemic.

The existing literature has focused on ambient temperature impacts on the infection and death of COVID-19 (Briz-Redón and Serrano-Aroca, 2020; Ma et al., 2020; Xie and Zhu, 2020; Yao et al., 2020). However, it remains unclear whether temperature affects non-COVID-19 and all-cause mortality during the pandemic period. The increasing deaths in the pandemic are not only directly caused by the virus infection but also indirectly caused by other social and environmental factors such as poor access to medical services and the lack of appropriate social and community support. Cold and heat could induce elevated risks of cardiovascular and respiratory diseases (Gasparrini et al., 2015b), and the vulnerability to temperature could be changed due to the socioeconomic conditions and healthcare quality (Achebak et al., 2019). Given the vulnerability of the socioeconomic changes in the pandemic and the poor acclimatization to extreme ambient temperatures particularly for the most vulnerable populations (e.g., living alone, chronically ill, and the elderly), the potential changes in the individual vulnerability to the temperature-mortality association during the pandemic is warranted. Therefore, the target of this study is to pinpoint the risks of all-cause mortality and non-COVID-19 mortality associated with ambient temperature in the COVID-19 pandemic year of 2020 across Italy, and then compare the risks with that in 2015–2019.

2. Methods

2.1. Data collection

We collected daily all-cause mortality data for 107 provinces in 20 regions of Italy from the Italian Institute of Statistics from January 1st, 2015, to November 30th, 2020, which covered about 95% of the Italian territory and population. The all-cause mortality at the province level was stratified by sex and age. To compare the effects of temperature on non-COVID-19 deaths during the pandemic in 2020, daily COVID-19-caused death counts at region level were collected from the Italian Department of Civil Protection from February 21st, 2020 to November 30th, 2020. The non-COVID-19 mortality at each region was calculated using all-cause death minus the COVID-19 death counts. The urban-rural classifications for the provinces of Italy were collected from the Eurostat maintained by European Commission (https://ec.europa.eu/eurostat/cache/RCI/#?vis=urbanrural.urb_typology&lang=en).

We collected the hourly ambient temperature and ambient dew point temperature (at 2 m above the land surface) with the spatial resolution of 0.1° × 0.1° from the ERA5 dataset (https://cds.climate.copernicus.eu/cdsapp#!/home). The maximum, minimum, and average daily temperature data were calculated based on those hourly observations. We calibrated the ERA5 daily mean temperature and ERA5 daily mean dew point temperature using their relationship with observations of weather stations by building random forest models. The calibration details can be found in another article (Ye et al., 2021). After calibration, the ERA5 daily mean temperature and ERA5 daily mean dew point temperatures were linked to the geographical center of each of the 794 municipalities based on longitude and latitude. Then, we aggregated them into province level by averaging observations of all municipalities within each province. We calculated daily mean relative humidity (RH) and specific humidity (SH) based on the calibrated ERA5 daily mean temperature and the dew point temperature (Cai, 2019). We also collected the daily monitor station data of particulate matter with diameters less than 2.5 μm (PM2.5) from World’s Air Quality Index Project and linked values of the nearest monitor station to the centre of each Italian province. All the data at the provincial level are aggregated to the regional level by averaging the observed values of all provinces in each region.

2.2. Statistics analysis

We employed a time-stratified case-crossover study design to interrogate the relationship of ambient temperature with deaths during the pandemic period 2020 and in its counterpart from 2015 to 2019 respectively. Conditional quasi-Poisson regression was applied to perform the time-stratified case-crossover design (Armstrong et al., 2014). Specifically, we matched the case with controls on the same day of the week, month, and province/region (for non-COVID-19 deaths) to hold the effect of intra-week variation, temporal and spatial variation (Guo et al., 2011). The lag effect was tested using a distributed lag non-linear model (DLNM) (Gasparrini et al., 2010). We used a natural cubic spline with 3 degrees of freedom for the temperature distribution and for lags days. A lag of up to 21 days was selected since previous studies have shown a long lag effect of cold and harvesting effect of heat (Gasparrini et al., 2015b; Guo et al., 2011). Therefore, we included our data from February 1st so that we included the first 21 days of the date when the first
COVID-19-related deaths appeared (on Feb. 21st, 2020) in the pandemic in Italy (Alicantro et al., 2020), and with a hard cut on November 30th. The daily RH with the same lag days, PM$_{2.5}$ concentration, daily COVID-19 confirmed cases, and the daily counts of ICU cases were included in the model to control their impacts on the temperature-mortality association.

To assess the possible modification effects of demographic factors on the associations between temperature and mortality, stratified analyses were conducted for sex and age groups (<64, 65–74, 75–84, and ≥85 years). We also explored the impact of urbanization on the temperature-mortality association by dividing Italy into 3 urban-rural regions, including predominantly rural regions (rural population: >50% of the total population), intermediate (rural population: 20–50% of the total population), and predominantly urban (rural population: <20% of the total population) (Fig. S1). The cumulative relative risks (RRs) of mortality (RRs along 21 lag days) related to extremely cold and heat (corresponding to the 2.5th and 97.5th percentiles of the temperature range, respectively) against the minimum mortality temperature (MMT) were calculated to identify the cold and hot effect (Gasparrini et al., 2015b). We set 19°C as MMT (reference temperature) based on our initial analyses using the method developed by a previous study to calculate the RRs (Gasparrini et al., 2015b). The random effect meta-regression methods were employed to test the statistical significance in RRs among the sex and age groups during the pandemic and pre-pandemic periods.

2.3. Sensitivity analysis

Sensitivity analyses were performed to examine the robustness of the results. We tested the variation of the temperature-mortality association by substituting every single year for the original study period 2015–2019. We modified the lag choices by varying the maximum lags to 18 and 24 days in the DLNM to check for any changes in the temperature-mortality associations. We also performed other sensitivity analyses by replacing RH with SH and using the daily maximum and minimum temperature separately to substitute the daily average temperature in our models to assess the robustness of the findings.

3. Results

There were 3,189,790 all-cause deaths from February 1st to November 30th during the years of 2015–2020 in Italy, which included 55,653 deaths from the coronavirus. Table 1 displays the comparison of descriptive statistics between the study period in 2020 and the average values in the same months during 2015–2019. There was no significant difference in the distribution of the ambient temperature between the two periods (Table 1 and Table 2). However, the RH and PM$_{2.5}$ in the pandemic 2020 were slightly lower than the same months during 2015–2019 (P < 0.001). The correlation about the atmospheric factors in the study period can be found in Fig. S2. As for the comparison of the daily average all-cause mortality counts in different sex and age groups, all subgroups in 2020 displayed statistically higher than that in 2015–2019 (Table 1). There were, on a daily average, 183 COVID-19 deaths and 1771 non-COVID-19 deaths in Italy in the study pandemic period. The COVID-19 death tolls account for 9.37% (55,653) of the all-cause mortality (593,977) in the study months in 2020.

Fig. 1 shows the daily changes of the death tolls by the coronavirus infection and all causes in 2020 and in its counterpart date from 2015 to 2019. Two obvious waves of COVID-19 infection hit Italy since the start of the COVID-19 outbreak in February 2020. As expected, Italy suffered more all-cause fatalities in the pandemic period than that in 2015–2019. However, more importantly, we found that the non-COVID-19 related death tolls followed a similar trend with the COVID-19 deaths in 2020, and the daily non-COVID-19 deaths at most of the time in 2020 were higher than the average deaths in the same period in 2015–2019.

| Table 1 | The basic distribution of meteorological conditions and daily average mortality in Italy from Feb.1st to Nov.30th, 2020 and its counterpart in 2015–2019. |
|---------|----------------------------------------------------------------------------------|
|          | 2015–2019                                                                                      | 2020                                                                                      | p-Value  |
|          | Mean | SD | Mean | SD |               | Mean | SD |               |
| Temperature (°C) | 15.54 | 6.71 | 15.61 | 6.49 | 0.067 |               |               |               |
| Relative Humidity (%) | 69.52 | 11.40 | 69.15 | 12.50 | <0.001 |               |               |               |
| PM$_{2.5}$ | 15.90 | 21.52 | 14.87 | 17.24 | <0.001 |               |               |               |
| Daily average mortality counts |                   |                   |                   |                   |               |                   |                   |
| Age groups |                   |                   |                   |                   |               |                   |                   |
| 0–64 | 193 | 18 | 197 | 30 | 0.003 |               |               |               |
| 65–74 | 231 | 23 | 264 | 64 | <0.001 |               |               |               |
| 75–84 | 507 | 54 | 568 | 152 | <0.001 |               |               |               |
| ≥85 | 782 | 97 | 925 | 216 | <0.001 |               |               |               |
| Sex |                   |                   |                   |                   |               |                   |                   |
| Women | 890 | 99 | 1002 | 207 | <0.001 |               |               |               |
| Men | 822 | 77 | 952 | 246 | <0.001 |               |               |               |
| Causes |                   |                   |                   |                   |               |                   |                   |
| COVID-19 death | NA | NA | 183 | 247 | NA |               |               |               |
| Non-COVID-19 deaths | 1712 | 170 | 1771 | 283 | <0.001 | 1712 | 170 | 1954 | 449 | <0.001 |

Note: the COVID-19 death in the pandemic period in 2020 from February 21th, 2020; SD: Standard deviation; Daily Average Mortality counts were rounded to integer values; we calculated the p-Value with independent Two-Sample t-Test.
We also compared the distribution of the daily average all-cause mortality rate in the pandemic (2020) and the non-pandemic period (2015–2019) (Fig. 2). The region of Lombardy in the north of Italy, which is the epicentre of the outbreak in the country, was mostly hit.

Fig. 3 shows overall cumulative exposure-response associations for the non-COVID-19 deaths and all-cause mortality in 2020 and 2015–2019, referring to the MMT of 19 °C. Generally, there were U-shaped curves of temperature-mortality associations for both periods. The risks of both all-cause mortality and non-COVID-19 mortality associated with cold environment (lower than 19 °C) in 2020 were higher than that in 2015–2019, while a similar increasing trend was found in high ambient temperatures above 19 °C.

Table 3 shows the risks of temperatures to mortality at extremely cold (2.5th percentile of temperature, i.e., 2 °C) and extremely heat (97.5th percentile of temperature i.e., 27 °C). The cumulative RR of all-cause mortality (1.63 (95%CI: 1.55–1.72)) and non-COVID-19 mortality (1.45 (95%CI: 1.31–1.61)) associated with extreme cold in 2020 in comparison with the MMT (19 °C) were higher than that in 2015–2019 with an RR of 1.19 (95%CI: 1.17–1.21). As for the association of mortality in extreme heat, the pandemic 2020 witnessed a similar cumulative RR for all-cause mortality and non-COVID-19 deaths compared with 2015–2019. With regards to the risks at extremely cold and heat in specific-age groups in the pandemic period, the 65–74 (RR of 1.82 (95%CI: 1.63–2.04)) and 75–84 age groups (RR of 1.85 (95%CI: 1.71–2.01)) reported significantly higher risks at extremely cold than the other two groups (with RR of 1.51 for 0–64 age group and 1.48 for ≥85 age group, respectively), while the risks at extreme heat were similar at different age and sex groups (Table 3).

Fig. 4 and Fig. 5 indicate the association between temperature and all-cause mortality stratified by sex, age, and urbanization rates.
Both males and females suffered a higher risk of mortality when exposing cold in 2020 than in 2015–2019, while males had a greater risk than females, with an RR of 1.74 and 1.54 at 2 °C respectively in the pandemic 2020 (Table 3). In terms of the age-specific comparison, except for the group with ages above 85 years old, the other three age groups experienced a significantly increased risk of mortality for cold in 2020 than 2015–2019. However, we did not find any significant differences for high

Fig. 2. The daily average all-cause mortality rate (per 100,000) in the pandemic (2020) and the non-pandemic period (2015–2019). Note: The population at the province level is based on 1st January 2020.

Fig. 3. Cumulative temperature–all-cause mortality and cumulative temperature-non-COVID-19 deaths associations along 21 lag days in the pandemic (2020) and the non-pandemic period (2015–2019). Note: Total death 2020: the all-cause deaths between February 1st and November 30th, 2020; Average total death 2015–2019: the average daily all-cause death in the period from February 1st to November 30th in 2015–2019; The non-COVID-19 deaths in the pandemic period in 2020: from February 21st to November 30th, 2020.

in 2020 and 2015–2019. Both males and females suffered a higher risk of mortality when exposing cold in 2020 than in 2015–2019, while males had a greater risk than females, with an RR of 1.74 and 1.54 at 2 °C respectively in the pandemic 2020 (Table 3). In terms of the age-specific comparison, except for the group with ages above 85 years old, the other three age groups experienced a significantly increased risk of mortality for cold in 2020 than 2015–2019. However, we did not find any significant differences for high
Guo et al., 2014; Vardoulakis et al., 2014). Some research literature concluded that cold contributed more temperature-attributable deaths in Italy; p-Values for differences: examining the statistically significance among subgroups with random effect meta-regression method.

### Table 3

| Age    | RR (95% CI) | p-Value for differences | RR (95% CI) | p-Value for differences |
|--------|-------------|------------------------|-------------|------------------------|
| 0–64   | 1.10 (1.04, 1.17) | reference | 1.51 (1.32, 1.72) | reference |
| 65–74  | 1.13 (1.08, 1.19) | 0.492     | 1.82 (1.63, 2.04) | 0.033     |
| 75–84  | 1.12 (1.08, 1.16) | 0.657     | 1.85 (1.71, 2.01) | 0.008     |
| ≥85    | 1.28 (1.24, 1.31) | <0.001    | 1.48 (1.39, 1.58) | 0.827     |
| Sex    |             |           |             |           |
| Female | 1.18 (1.15, 1.21) | reference | 1.54 (1.44, 1.64) | reference |
| Male   | 1.20 (1.16, 1.23) | 0.51      | 1.74 (1.63, 1.86) | 0.007     |
| Total  | 1.19 (1.17, 1.21) | NA        | 1.63 (1.55, 1.72) | NA        |
| Non-COVID-19 deaths | NA | NA | 1.45 (1.31, 1.61) | NA |

Note: Extremely Cold: the average daily temperature at 2 °C; Extremely Hot: the average daily temperature at 27 °C; RR: Relative Risk, overall cumulative relative risk of mortality in previous 21 days, compared with 19 °C; 2020: the pandemic period between February 1st and November 30th, 2020; 2015–2019: the period in the same months in 2015–2019; The non-COVID-19 deaths: using the daily all-cause deaths minus daily COVID-19 deaths in Italy; p-Values for differences: examining the statistically significance among subgroups with random effect meta-regression method.

ambient temperature in each subgroup (Fig. 4). For the associations in different urban-rural regions (Fig. 5), the results of predominantly urban and intermediate regions in Italy indicated a similar trend with higher cold effects in 2020 than 2015–2019, but with a similar hot effect. By contrast, in predominantly rural regions, the temperature-mortality association for cold was reversed by the pandemic and displayed a higher hot effect in 2020 than in 2015–2019.

As for the results of sensitivity analysis, our main results were robust when we replaced 2015–2019 with every single year from 2015 to 2019 (Fig. S3), and when we varied the maximum lag days from 21 to 18 and 24 days in our model (Fig. S4). Our results were stable when replacing RH with SH (Fig. S5) and substituting the daily maximum and minimum temperature separately for the daily average temperature in our models (Fig. S6).

### 4. Discussion and conclusions

Our study investigated the difference in temperature-mortality associations in the pandemic and non-pandemic periods. The findings indicated that Italy experienced higher cold-related all-cause and non-COVID-19 mortality in the pandemic 2020 in comparison to the counterpart from 2015 to 2019, while no difference was found for the effects of heat. Furthermore, males suffered more risk of cold-related mortality than females in the pandemic, but no significant changes in risks of mortality were found for people aged above 85 years between 2020 and 2015–2019. The changes in temperature-mortality association for rural-urban differences were significant in the pandemic period.

It is well-documented that cold and heat are responsible for the risk of mortality (Gasparrini et al., 2015a; Gasparrini et al., 2015b; Guo et al., 2014; Vardoulakis et al., 2014). Some research literature concluded that cold contributed more temperature-attributable mortality than heat (Gasparrini et al., 2015b; Vardoulakis et al., 2014). For instance, Gasparrini et al. assessed the all-cause mortality risk attributed to cold and hot for 384 locations in 13 countries around the world. It was observed that Italy experienced a higher temperature-related mortality burden caused by cold (9.35%) than by heat (1.62%) from 1987 to 2010 (Gasparrini et al., 2015b). Consistent with this study, we found a lower heat-related mortality risk (with RR of 1.12 and 1.15 separately) than cold (with RR of 1.19 and 1.63 separately) in the non-pandemic (2015–2019) and pandemic study periods in 2020, even though the results could not be directly compared with previous research due to the different MMT and study period (from February to November in this study).

The individual vulnerability to ambient temperature may be changed in the pandemic period via a range of physiological, behavioural, and socioeconomic variations. A current systematic review concluded that apart from the individual-level factors like age and sex, community-level factors such as socioeconomic status could affect the temperature-mortality association (Son et al., 2019). Italy has seen significant socioeconomic inequalities such as educational disparity and unemployment in the context of the COVID-19 pandemic (Consolazio et al., 2021), which played a crucial role in vulnerability to high and low temperatures (Mari-Dell’Olmo et al., 2019). Our results show that a higher cold-related mortality risk during the 2020 COVID-19 pandemic than the same months during 2015–2019 but with no difference for the changes in the heat effects. Given no huge difference in climate characteristics with previous
years, the individual vulnerability to the low temperature-mortality association in the pandemic seemed to be changed in Italy. 

To distinguish the COVID-19 deaths from the all-cause mortality, we explored the association between temperature and non-COVID-19 mortality. The results suggested a higher risk of non-COVID-19 mortality for cold exposure in the pandemic period, which further indicated the potential changes in people's vulnerability to temperature for the non-COVID-19 mortality. The possible explanation for such change could be the adaptation to ambient temperature (Gasparrini et al., 2017; Schwartz et al., 2015). Specifically, the variation of temperature-mortality association mainly relies on two pathways: an intrinsic adaptation by a physiological acclimatization response, and the extrinsic adaptation due to externally driven factors such as socioeconomic and demographic conditions and public health services (Achebak et al., 2020; Vicedo-Cabrera et al., 2018). Especially for the time when the COVID-19 virus spread quickly and widely, extrinsic factors such as the healthcare resources availability and the shortage of healthcare for the treatment of temperature-related diseases could change the vulnerability of patients to temperature. For example, the rapid surge of confirmed COVID-19 cases has raised a serious challenge to the Italian national health system (Remuzzi and Remuzzi, 2020). Because of the lack of medical resources and reorganization of the health care systems to the enormous increase in acutely COVID-19 patients (Ji et al., 2020), some patients with acute diseases got worse due to the cold environment and even died while awaiting admission in the pandemic (Emanuel et al., 2020).

Furthermore, another possible explanation is that the adverse psychosocial effects of pandemics may be related to the individuals' intrinsic physiological and psychological vulnerability to cold (Guessoum et al., 2020). For example, research revealed that social exclusion could make people feel cold (Zhong and Leonardelli, 2008), which may exacerbate the risk of cold-related mortality. Several studies also observed that ambient temperatures are associated with the increase in emergency department visits for mental illness,
suicides, and self-reported days of poor mental health (Mullins and White, 2019; Xue et al., 2019). Restrictive social containment measures like stay-at-home orders may aggravate the adverse psychological outcomes and mental disorders, resulting in excess cold-related mortality (Pfefferbaum and North, 2020).

We did not find a significant difference in the heat-mortality association between the pandemic and non-pandemic periods. One of the potential reasons is the changed pandemic preventive status and activities in the summer of 2020. For example, Italy, from June to mid-September, saw a slowly spread of new COVID-19 cases. Accordingly, few restrictions like free movement and the reopen of social care systems were gradually restored in this period (National Statistical Institute (Istat) and the Institute Superiore di Sanità (Iss), 2020). As a result, no change in people’s vulnerability to heat was found in the pandemic summer in comparison with the non-pandemic period.

The effects of temperature for different sex and ages are largely driven by a thermoregulatory pathway. Some studies suggested that men are more likely to be susceptible to cold than women because of a larger fall in core body temperature when being exposed to the colder temperature, whereas other studies reported the opposite (Achebak et al., 2019; Moghadamnia et al., 2017). The body temperature maintenance for males and females may differ with health and socioeconomic conditions (Moghadamnia et al., 2017). With regards to the age-specific differences in thermoregulatory with cold exposure, the main physiological response to low temperature for the elderly is to decrease metabolic hot production and increase peripheral vasoconstriction in comparison with younger individuals who more rely on external conditions or do physical exercise (Achebak et al., 2019; Stocks et al., 2004). Additionally, multiple factors other than physiological mechanisms could explain the disparity in the temperature-mortality association between different age groups. One possible explanation for the pronounced gap in the RRs between the above 85 age group and other older groups is the health-related behaviours in the pandemic. For example, the older individuals may be more concerned about their vulnerability to COVID-19 infection and are more willing to conduct personal protection measures such as wearing masks and staying indoors and thus to avoid cold exposures and infectious diseases.

Urbanization features also play a crucial role in the transmission of COVID-19 (Li et al., 2021) as well as the vulnerability to cold and heat (Hu et al., 2019). Hu et al. indicated that rural residents tend to be more sensitive to cold and hot than urban citizens in China (Hu et al., 2019). However, the vulnerability to temperature may be changed in the pandemic due to the differences in socioeconomic impacts and COVID-19 related measures and governance (Sharifi and Khavarian-Garmsir, 2020). Our results showed that except for the rural regions, urban and intermediate regions in Italy witnessed a significantly higher cold-related mortality risk in the pandemic than non-pandemic period. The urban-rural differences in the vulnerability to cold and heat in the pandemic may be more related to the higher proportion of the vulnerable population and population density, more severe socioeconomic disruption and inequalities, and stricter urban management (Tricarico and De Vidovich, 2021). However, further studies are warranted to explore such impacts on the individual vulnerability in urban-rural regions.

Even though we were unable to make any inference in terms of the possible mechanism pathways governing the changed association between cold exposure and excess mortality in the pandemic, the potential biological mechanisms of cold with the increased mortality risks may mainly stem from cardiovascular and respiratory effects (Song et al., 2017). Cold exposure could induce an increase in the angiotensin-II levels in plasma, blood viscosity, arterial pressure, and platelet and red cell counts, which would lead to increased blood pressure and the elevated risks of hypertension and cardiovascular diseases (Analitis et al., 2008; Keatinge et al., 1984). The mechanisms underlying the respiratory effects may be associated with the effect of cold on the reduction of respiratory defences against infection and other immunological reactions (Eccles, 2002). Meanwhile, low ambient temperature could affect the
transmission of viruses and enhance the rates of respiratory virus infection (Pica and Bouvier, 2014).

There are some limitations in this study. Even though we included non-COVID-19 deaths, the analysis of the other disease-specific mortality and the patient-specific non-COVID-19 deaths were missing due to the data unavailability. Therefore, we did not know the extent of the temperature impact on certain disease-specific mortality in the pandemic. In addition, the intervention measures like stay-at-home rules in the different pandemic stages may influence the exposure to temperatures and modify human behaviours, which is warranted to explore in further analysis. An additional limitation is that this is an ecological study without individual data. Therefore, exposure misclassification is a potential concern. For example, the aggregated ambient temperature at the provincial level does not necessarily remain consistent for individuals, specifically for people who may reduce the cold exposure because of keeping the stay-at-home orders during the pandemic.

In conclusion, our findings suggest that the COVID-19 pandemic strengthened the impacts of ambient temperature on both the all-cause and non-COVID-19 in Italy, especially for cold exposure. This means that using the historical temperature-mortality relationship may not present the impacts of temperatures in the current period. To date, there is no indication that our life will transition to normalcy even though the administration of the COVID-19 vaccines is beginning. Some restrictive social containment measures may continually affect our lives and behaviours in the foreseeable future. Therefore, we would expect our findings to enable public health agencies to take early actions such as making preparedness for developing early cold warning systems, and giving special attention and health support to the vulnerable group, to avoid unexpected cold-related excess mortality in the future.

Contributors

YG and SL obtained funding. YG designed the study; RX, TY, and WY were involved in data collecting, cleaning, and verification; YG and WY analyzed the data; WY drafted the manuscript. SL, YG, and CH contributed to the interpretation of the results and critical revision of the manuscript for important intellectual content and approved the final version of the manuscript. ZC and JS reviewed the draft and provided COVID-19 related data. All authors have read and approved the final manuscript. YG and SL are the study guarantors.

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Data sharing

No additional data are available.

Declaration of Competing Interest

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

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.uclim.2021.100948.

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