The association between temperature variability and cause-specific mortality: Evidence from 47 Japanese prefectures during 1972 2015

著者（英）	Chaochen Ma, Jun Yang, Shoji F. Nakayama, Yasushi HONDA
journal or publication title	Environment International
volume	127
page range	125-133
year	2019-06
権利	(C) 2019 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/BY-NC-ND/4.0/)
URL	http://hdl.handle.net/2241/00157183

doi: 10.1016/j.envint.2019.03.025

Environment International 127 (2019) 125–133

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

The association between temperature variability and cause-specific mortality: Evidence from 47 Japanese prefectures during 1972–2015

Chaochen Ma[a,*,1], Jun Yang[b,1], Shoji F. Nakayama[a], Yasushi Honda[c,**]

[a] Center for Health and Environmental Risk Research, National Institute for Environmental Studies, 16-2 Onogawa, Tsukuba, Ibaraki 305-8506, Japan
[b] Institute for Environmental and Climate Research, Jinan University, Guangzhou 511443, China
[c] Faculty of Health and Sport Sciences, University of Tsukuba, Tsukuba, Japan

ARTICLE INFO

Handling Editor: Zorana Jovanovic Andersen

Keywords:
Climate change
Temperature variability
Cause-specific mortality
Japan

ABSTRACT

Background: In the context of climate change, extreme temperature events are known to be associated with increased mortality risk. However, data about the mortality risk related to temperature variability (TV) accounting for both intra- and inter-day variations in temperature are limited.
Objectives: The present study aims to quantify the associations between TV and cause-specific mortality in Japan, evaluate whether the effects of TV are modified by prefecture-level characteristics and examine the temporal trend in mortality risk of TV.
Methods: Data on daily all-cause and 11 cause-specific mortality and meteorological variables in 47 Japanese prefectures from 1972 to 2015 were collected. TV was defined as the standard deviation of daily minimum and maximum temperatures during exposure days. A quasi-Poisson regression model combined with a distributed lag non-linear model was firstly applied to assess the prefecture-specific mortality effects of TV, adjusting for potential confounders. The pooled effects of TV at the national level were then obtained via a meta-analysis through the restricted maximum-likelihood estimation. Potential effect modification by prefecture characteristics was firstly examined using a meta-regression analysis, and the joint modification of season and humidity was then evaluated after including product terms in two-stage analyses. Finally, the temporal trend in TV effects was evaluated by a random-effect meta regression model after obtaining the prefecture-year-specific effects.
Results: TV had significant adverse effects on all-cause and cause-specific mortality. The effects of TV were more detrimental to those with asthma and senility. In general, the estimates of mortality risk increased with longer exposure days. A 1 °C increase in TV at 0–7 days of exposure was associated with a 0.9% (95% confidence intervals: 0.82%–0.98%) increase in all-cause mortality. All-cause mortality risk of TV showed a decreasing trend during our study period. TV effects were larger in densely populated prefectures and on warm and humid days.
Conclusions: TV-related death is a significant issue in Japan that requires effective interventions.

1. Introduction

Climate change is a major public health concern in the 21st century (IPCC, 2014). The most direct way in which climate change affects human systems is via extreme temperature events, including heat wave, cold spell, or both (Hajat et al., 2014). Over the past two decades, numerous studies have provided evidence about temperature-related mortality in different countries (Basu, 2009; O'neill and Ebi, 2009; Huang et al., 2013; Thomas et al., 2014; Vardoulakis et al., 2014; Gasparrini et al., 2015b). The relationship between temperature and mortality is often depicted as U-, V- or J-shaped, with increases in mortality at high or low temperatures (Gasparrini et al., 2015b; Vicedo-Cabrera et al., 2016). However, these studies can only be used to "average warming trend".

In light of climate change, some climate models have observed a slightly decreasing trend of temperature variability (TV) in some

* Correspondence to: C. Ma, Center for Health and Environmental Risk Research, National Institute for Environmental Studies, 16-2 Onogawa, Tsukuba, Ibaraki 305-8506, Japan.
** Correspondence to: Y. Honda, Faculty of Health and Sport Sciences, University of Tsukuba, 1-1-1 Tennodai (Comprehensive Res Build D), Tsukuba 305-8577, Japan.
E-mail addresses: mcc1988forward@gmail.com (C. Ma), honda.yasushi.fn@u.tsukuba.ac.jp (Y. Honda).
[1] Co-first authors.

https://doi.org/10.1016/j.envint.2019.03.025
Received 31 October 2018; Received in revised form 10 March 2019; Accepted 10 March 2019
Available online 23 March 2019

Table 1
Descriptive data on daily all-cause mortality, mean temperature and temperature variability (from 0–1 to 0–7 days of exposure) across 47 Japanese prefectures during 1972–2015.

Prefecture	All-cause	Temperature (°C)	Temperature variability (°C)						
			0–1 days	0–2 days	0–3 days	0–4 days	0–5 days	0–6 days	0–7 days
Hokkaido	113 ± 29	8.9 ± 9.5	4.7	4.6	4.6	4.7	4.7	4.7	4.7
Aomori	34 ± 9	10.3 ± 8.9	4.9	4.8	4.8	4.8	4.8	4.8	4.8
Iwate	34 ± 46	10.3 ± 9.3	5.6	5.5	5.4	5.4	5.4	5.4	5.4
Miyagi	45 ± 83	12.4 ± 8.3	4.7	4.6	4.6	4.6	4.6	4.6	4.6
Akita	31 ± 8	11.7 ± 9.0	4.6	4.5	4.5	4.5	4.5	4.5	4.5
Yamagata	31 ± 8	11.7 ± 9.3	5.6	5.5	5.4	5.4	5.4	5.4	5.4
Fukushima	49 ± 19	13.0 ± 8.8	5.5	5.4	5.4	5.4	5.4	5.4	5.4
Ibaraki	59 ± 17	13.7 ± 8.1	5.8	5.6	5.6	5.6	5.6	5.6	5.6
Tochigi	41 ± 12	13.8 ± 8.5	6.0	5.8	5.8	5.8	5.8	5.8	5.8
Gunma	42 ± 12	14.5 ± 8.5	5.7	5.6	5.5	5.5	5.5	5.5	5.5
Saitama	101 ± 38	14.9 ± 8.4	5.9	5.7	5.7	5.6	5.6	5.6	5.6
Chiba	93 ± 33	15.7 ± 7.7	4.5	4.4	4.4	4.4	4.4	4.4	4.4
Tokyo	211 ± 56	16.2 ± 7.8	4.4	4.3	4.3	4.3	4.3	4.3	4.3
Kanagawa	125 ± 45	15.8 ± 7.6	4.4	4.3	4.3	4.3	4.3	4.3	4.3
Niigata	58 ± 14	13.8 ± 8.7	4.3	4.2	4.2	4.2	4.3	4.3	4.3
Toyama	26 ± 7	14.0 ± 8.8	5.0	4.9	4.9	4.9	4.9	4.9	4.9
Ishikawa	25 ± 7	14.6 ± 8.6	4.7	4.7	4.6	4.7	4.7	4.7	4.7
Fukui	19 ± 6	14.5 ± 8.8	5.1	5.0	5.0	5.0	5.0	5.0	5.0
Yamanashi	20 ± 6	14.6 ± 8.6	6.4	6.2	6.1	6.1	6.1	6.1	6.1
Nagano	51 ± 12	11.9 ± 9.5	5.9	5.7	5.7	5.7	5.7	5.7	5.7
Gifu	43 ± 12	15.8 ± 8.6	5.5	5.3	5.3	5.3	5.3	5.3	5.3
Shizuoka	73 ± 21	16.6 ± 7.4	5.1	4.9	4.9	4.9	4.9	4.9	4.9
Aichi	117 ± 34	15.7 ± 8.5	5.3	5.1	5.1	5.1	5.1	5.1	5.1
Mie	40 ± 11	15.8 ± 8.2	4.6	4.5	4.5	4.4	4.4	4.5	4.5
Shiga	24 ± 7	14.7 ± 8.5	4.7	4.6	4.5	4.5	4.5	4.5	4.5
Kyoto	53 ± 13	15.9 ± 8.6	5.5	5.3	5.3	5.3	5.3	5.3	5.3
Osaka	157 ± 41	16.8 ± 8.3	4.7	4.6	4.6	4.6	4.6	4.6	4.6
Hyogo	109 ± 47	16.3 ± 8.2	4.4	4.3	4.2	4.2	4.2	4.3	4.3
Nara	27 ± 8	14.9 ± 8.4	6.1	5.9	5.8	5.8	5.8	5.8	5.8
Wakayama	27 ± 7	16.6 ± 8.1	4.8	4.6	4.6	4.6	4.6	4.6	4.6
Tottori	15 ± 5	14.9 ± 8.4	5.5	5.3	5.3	5.3	5.3	5.3	5.3
Shimane	21 ± 6	14.8 ± 8.2	5.1	4.9	4.9	4.9	4.9	4.9	4.9
Okayama	45 ± 11	15.9 ± 8.6	5.4	5.2	5.2	5.1	5.1	5.1	5.1
Hiroshima	60 ± 15	15.9 ± 8.3	5.0	4.9	4.8	4.8	4.8	4.8	4.8
Yamaguchi	39 ± 10	15.3 ± 8.4	5.9	5.7	5.6	5.6	5.6	5.6	5.6
Tokushima	21 ± 6	16.5 ± 7.9	4.6	4.5	4.4	4.4	4.4	4.4	4.4
Kagawa	24 ± 7	16.2 ± 8.3	5.1	5.0	5.0	4.9	4.9	4.9	4.9
Ehime	37 ± 9	16.3 ± 8.0	5.0	4.8	4.8	4.8	4.8	4.8	4.8
Kochi	23 ± 6	16.9 ± 7.7	5.6	5.4	5.3	5.3	5.3	5.3	5.3
Fukuoka	99 ± 25	16.9 ± 7.8	4.5	4.4	4.4	4.4	4.4	4.4	4.4
Saga	21 ± 6	16.5 ± 8.2	5.4	5.3	5.2	5.2	5.2	5.2	5.2
Nagasaki	37 ± 9	17.1 ± 7.6	4.3	4.2	4.2	4.2	4.2	4.2	4.3
Kumamoto	43 ± 11	16.8 ± 8.3	5.8	5.6	5.6	5.6	5.6	5.6	5.6
Oita	30 ± 8	16.3 ± 7.7	5.1	5.0	4.9	4.9	4.9	4.9	4.9
Miyazaki	27 ± 8	17.5 ± 7.4	5.4	5.2	5.2	5.2	5.2	5.2	5.2
Kagoshima	47 ± 11	18.3 ± 7.5	5.0	4.9	4.8	4.8	4.8	4.8	4.8
Okinawa	20 ± 7	22.9 ± 4.7	3.0	2.9	2.9	2.9	3.0	3.0	3.0

regions, including Japan over the past half-century (Schär et al., 2004; Bathiany et al., 2018). However, given the super-aging of the population, such as Japan, the harmful health effects of TV should not be neglected. To date, most studies only quantified the mortality risk related to either intra-day TV (diurnal temperature range) or inter-day TV (temperature change between two neighboring days) (Lin et al., 2013; Yang et al., 2013; Vicedo-Cabrera et al., 2016). However, one TV measure can be confounded by the other and simultaneous consideration of both is necessary. As such, a composite TV indicator accounting for both intra- and inter-day TV was developed recently (Guo et al., 2016). Still, the cause-specific mortality risk of TV and effect modification of the association between TV and mortality by city-level characteristics are not well elucidated. Therefore, further epidemiological evidence is needed to comprehensively understand this issue.

The purpose of this study is to quantify the short-term TV effects on mortality, test the effect modification by prefecture-level characteristics and examine temporal trend in mortality risk of TV using a national data set covering 47 Japanese prefectures from 1972 to 2015.

2. Materials and methods

2.1. Data collection

Japan is composed of 47 prefectures. In each prefecture, there are further three administrative divisions: cities, towns and villages. We collected daily records for all-cause and 11 cause-specific mortality from January 1, 1972 to December 31, 2015 across all 47 Japanese prefectures from the Ministry of Health, Labor and Welfare of Japan. The mortality data for Okinawa were collected one year later, from January 1, 1973 to December 31, 2015. The International Classification of Diseases, 8th Revision (ICD-8), ICD-9 and ICD-10 codes were used from 1972 to 1978, 1979 to 1994 and 1995 to 2015, respectively. Data on cause-specific mortality were obtained according to the ICD codes: circulatory disease, ICD-8: 390–458, ICD-9: 390–459, and ICD-10: I00–I99; respiratory disease, ICD-8: 460–519, ICD-9: 460–519, and ICD-10: J00–J99; renal disease, ICD-8: 580–599, ICD-9: 580–599, and ICD-10: N00–N39; ischemic heart disease (IHD), ICD-8: 410–414, ICD-9:

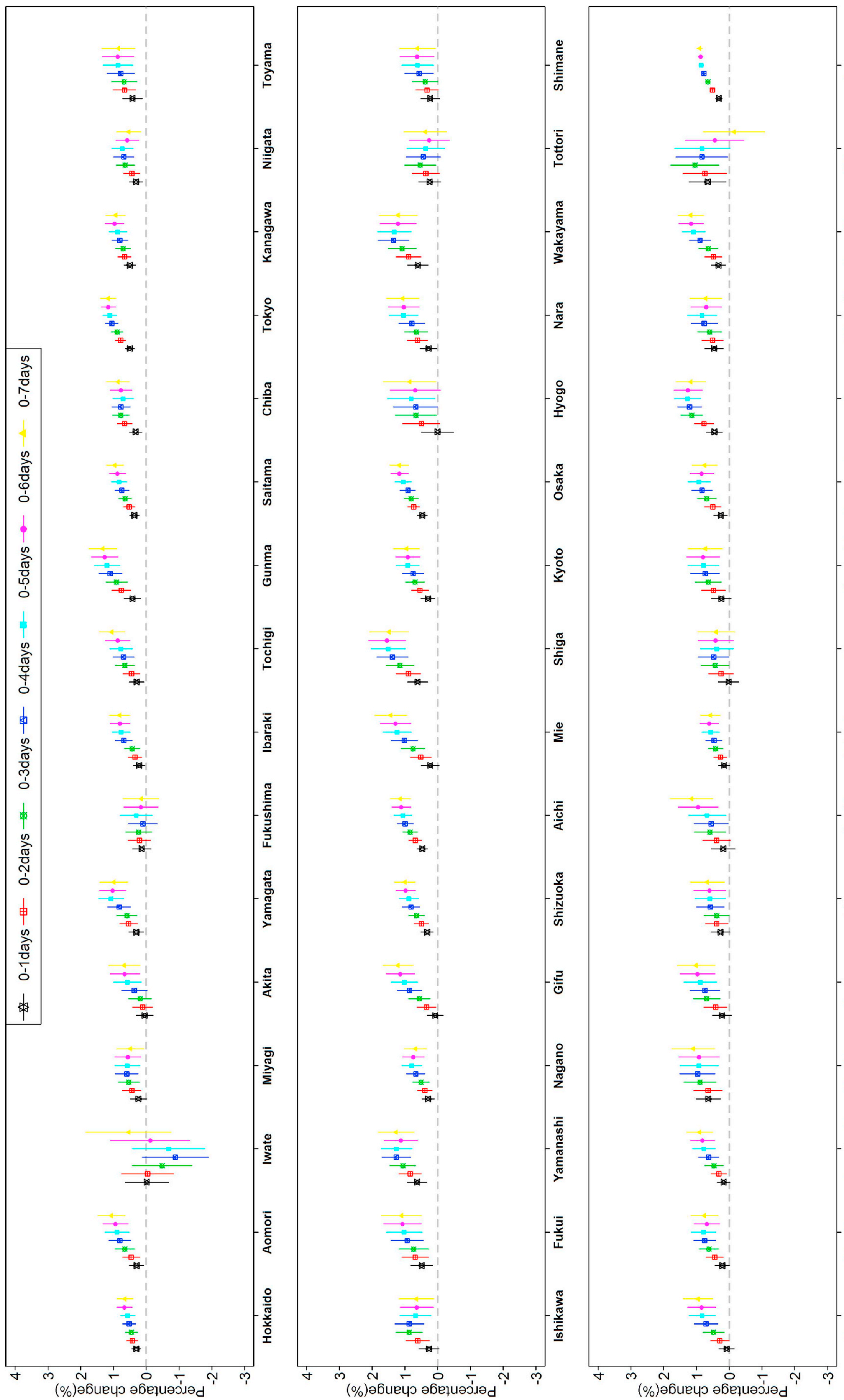

Fig. 1. Prefecture-specific and the pooled effect estimates of per 1 °C increase in temperature variability on all-cause mortality at different exposure days.

Table 2
The pooled percent increase (mean and 95% CI[a]) in cause-specific mortality associated with 1 °C increase in temperature variability at different exposure days across 47 Japanese prefectures during 1972–2015.

Variable	0–1 days	0–2 days	0–3 days	0–4 days	0–5 days	0–6 days	0–7 days
All-cause	0.32 (0.27,0.36)	0.51 (0.46,0.57)	0.65 (0.59,0.71)	0.77 (0.70,0.84)	0.85 (0.78,0.92)	0.87 (0.80,0.95)	0.90 (0.82,0.98)
Circulatory	0.27 (0.20,0.33)	0.52 (0.43,0.60)	0.71 (0.61,0.80)	0.89 (0.81,0.98)	1.00 (0.91,1.10)	1.07 (0.97,1.17)	1.11 (1.01,1.22)
Respiratory	0.29 (0.18,0.40)	0.57 (0.44,0.70)	0.80 (0.65,0.95)	1.00 (0.84,1.16)	1.11 (0.93,1.30)	1.15 (0.95,1.35)	1.24 (1.04,1.45)
Cerebrovascular	0.24 (0.16,0.32)	0.54 (0.45,0.63)	0.73 (0.63,0.84)	0.90 (0.78,1.01)	0.98 (0.85,1.10)	1.04 (0.91,1.18)	1.09 (0.94,1.24)
IHD	0.29 (0.14,0.44)	0.47 (0.28,0.65)	0.64 (0.44,0.83)	0.80 (0.61,1.00)	0.95 (0.76,1.14)	0.98 (0.76,1.20)	1.02 (0.78,1.26)
Pneumonia	0.30 (0.16,0.43)	0.52 (0.35,0.69)	0.76 (0.58,0.94)	0.95 (0.76,1.14)	1.08 (0.88,1.29)	1.11 (0.89,1.32)	1.18 (0.97,1.39)
Asthma	0.24 (−0.18,0.67)	0.65 (0.16,1.14)	1.13 (0.58,1.69)	1.57 (0.95,2.18)	1.59 (0.92,2.26)	1.74 (1.03,2.46)	1.83 (1.07,2.60)
Renal	0.33 (0.12,0.53)	0.59 (0.35,0.83)	0.82 (0.53,1.12)	1.01 (0.70,1.31)	1.11 (0.77,1.45)	1.10 (0.73,1.47)	1.00 (0.57,1.43)
Cerebral hemorrhage	0.17 (0.04,0.30)	0.40 (0.23,0.57)	0.58 (0.39,0.76)	0.63 (0.42,0.84)	0.69 (0.45,0.93)	0.63 (0.39,0.88)	0.62 (0.34,0.90)
Cerebral infarction	0.30 (0.17,0.43)	0.67 (0.51,0.82)	0.86 (0.69,1.02)	1.05 (0.87,1.24)	1.15 (0.96,1.35)	1.30 (1.09,1.52)	1.39 (1.16,1.61)
Senility	0.38 (0.22,0.55)	0.81 (0.60,1.02)	1.23 (0.98,1.48)	1.42 (1.15,1.69)	1.60 (1.31,1.89)	1.73 (1.42,2.04)	1.82 (1.49,2.16)
COPD	0.08 (−0.26,0.43)	0.41 (0.01,0.82)	0.58 (0.14,1.02)	0.72 (0.18,1.27)	0.71 (0.13,1.29)	0.86 (0.26,1.47)	0.85 (0.23,1.47)

[a] CI, confidence intervals.

410–414, and ICD-10: I20–I25; cerebrovascular disease, ICD-8: 430–438, ICD-9: 430–438, and ICD-10: I60–I69; cerebral hemorrhage, ICD-8: 430–431, ICD-9: 430–432, and ICD-10: I60–I62; cerebral infarction, ICD-8: 432–435 or 437, ICD-9: 433–435 or 437, and ICD-10: I65–I66 or I63; senility, ICD-8: 794, ICD-9: 797, and ICD-10: R54; pneumonia, ICD-8: 480–486, ICD-9: 480–486, and ICD-10: J12–J18; asthma, ICD-8: 493, ICD-9: 493, and ICD-10: J45–J46; and chronic obstructive pulmonary disease (COPD), ICD-8: 491–492, ICD-9: 491–492 or 496, and ICD-10: J41–J44. Most of the selected diseases are listed as the "top killers" in Japan, according to the Ministry of Health, Labor and Welfare, Japan (Portal Site of Official Statistics of Japan, 2017). Among the 11 causes of death, senility has aroused much concern due to its increasing death rate in recent years (Sakamitsu, 2018).

Data on weather variables were obtained from the Japan Meteorological Agency. Daily mean, minimum and maximum temperatures (°C), and mean relative humidity (RH) (%) were calculated as the 24-h averages of hourly measurements obtained from a single monitoring station located in the capital city of each prefecture (except for Shiga prefecture and Saitama prefecture, where the monitoring stations from Hikone city and Kumagaya city were selected, respectively).

We also acquired information on prefecture-level data. Geographical data (latitude and longitude) were obtained from the Geospatial Information Authority of Japan (http://www.gsi.go.jp/ENGLISH/index.html). Socioeconomic data, collected from Japan's 2012 population census, which included unemployment rate, percentage of individuals older than 75 years, population, population density, and GDP, were downloaded from the Portal Site of Official Statistics of Japan (https://www.e-stat.go.jp/en). All the prefecture-level data are shown in Table A1.

2.2. Definition of TV

In this study, we used a newly proposed indicator that can account for both intra- and inter-day temperature variations by calculating the standard deviation (SD) of the minimum and maximum temperatures over exposure days (Guo et al., 2016). For instance, TV exposure for the current and preceding day can be calculated as TV_{0-1} = SD (Mintemplag0, Maxtemplag0, Mintemplag1, Maxtemplag1); TV exposure for the current and preceding 2 days can be calculated as TV_{0-2} = SD (Mintemplag0, Maxtemplag0, Mintemplag1, Maxtemplag1, Mintemplag2, Maxtemplag2). Moreover, we compared mortality risk by changing the exposure days from TV_{0-1} to TV_{0-7}.

2.3. Statistical analysis

Two-stage analyses were performed to quantify the associations between TV and mortality as well as the effect modification by prefecture-level factors.

2.3.1. First-stage analysis

In the first stage, a time-series quasi-Poisson regression model allowing for over-dispersion combined with a distributed lag non-linear model (DLNM) was applied to evaluate the associations between TV and mortality for each prefecture (Bhaskaran et al., 2013; Gasparrini et al., 2015b). Briefly, a natural cubic spline of time with seven degrees of freedom (*dfs*) per year to control for long-term and seasonal trend in mortality; a natural cubic spline with three *dfs* for RH; a categorical variable for day of the week and a binary variable for the public holidays (Ban et al., 2017). In addition, DLNM was used to control for the nonlinear and delayed effects of temperature on mortality (Gasparrini et al., 2015b). Specifically, a natural cubic spline with four *dfs* was used to describe the exposure-response and lag-response relationships, respectively. The maximum lag was set to 21 days to consider both heat and cold effects (Yi and Chan, 2015). These modeling strategies were adopted by previous studies on both global and regional scales (Yang et al., 2012; Guo et al., 2014; Ma et al., 2014).

Previous studies have indicated that the association between TV and mortality was linear (Guo et al., 2016; Cheng et al., 2017; Zhang et al., 2017), and this linear relationship still held for most of the densely populated Japanese prefectures in our initial analysis (Fig. A1). Thereby, we separately evaluated the effect of TV at different exposure days from TV_{0-1} to TV_{0-7} (Guo et al., 2016). The optimal length of exposure was based on the minimum value of Akaike information criterion (Q-AIC) for all-cause and cause-specific mortality across 47 prefectures.

2.3.2. Second-stage analysis and effect modification

To obtain the overall effects of TV in Japan, we pooled the estimated prefecture-specific mortality risk of TV via a meta-analysis through the restricted maximum-likelihood estimation (Viechtbauer, 2010). The prefecture-specific and pooled mortality risk of TV was expressed as the percentage increase in mortality associated with 1 °C increase in TV. Furthermore, we investigated effect modification by prefecture-level characteristics using the mixed effects meta-regression model (Ma et al., 2015; Yang et al., 2018). The heterogeneity across prefectures was obtained using the Cochran Q test and I^2 statistics (Gasparrini et al., 2012; Ma et al., 2015; Yang et al., 2018). Also, to investigate the possible joint effect modification by season and RH, we created two binary variables. One binary variable was for season, with 1 for the warm season (from May to October) and 0 for the cold season (from November to April). The other variable was for daily RH levels, with 1 for humid days and 0 for dry days. The median value of daily RH was chosen as the cutoff point. Then, four binary variables were produced for the combinations of season and RH: warm season with high RH days (warm & humid days), warm season with low RH days (warm & dry

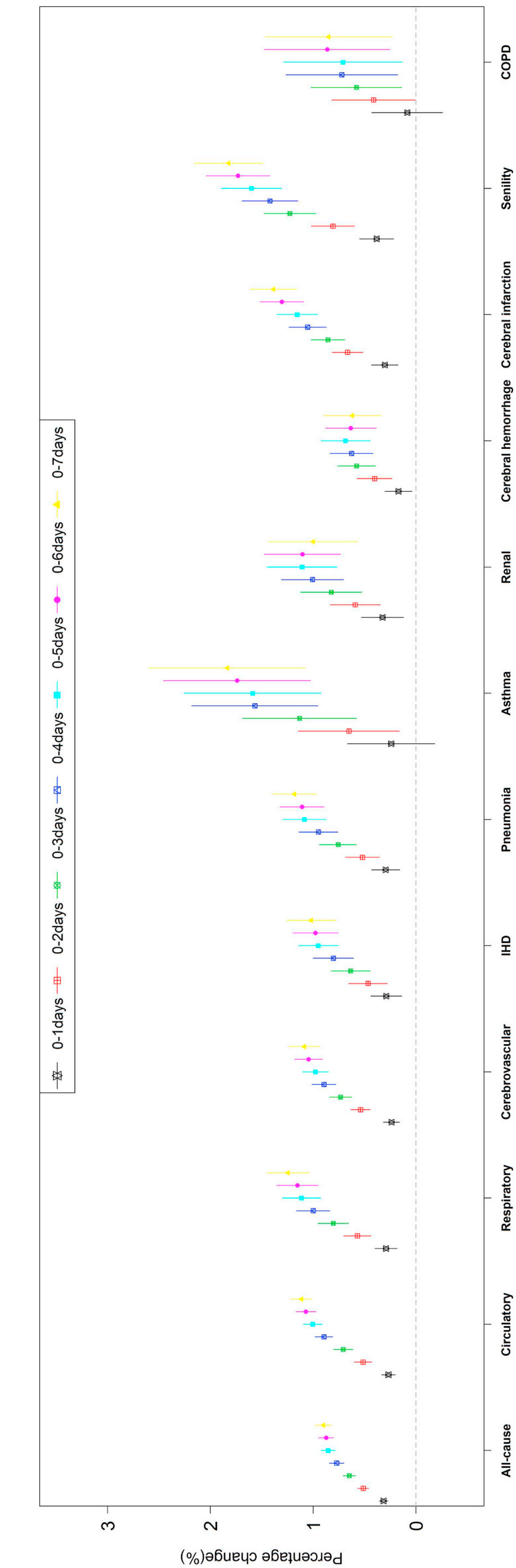

Fig. 2. The pooled effect estimates of per 1 °C increase in temperature variability on cause-specific mortality at different exposure days.

days), cold season with high RH days (cold & humid days) and cold season with low RH days (cold & dry days). The product term of TV and these binary variables were introduced in the two-stage analytic approach to explore the possible joint modification of season and RH level.

2.3.3. *Temporal variation in TV-mortality association*

We examined the temporal variation in TV-mortality association during 1972–2015 using a two-stage analysis. Firstly, the prefecture-year-specific association between $TV_{0–7}$ and all-cause mortality was evaluated using the abovementioned quasi-Poisson regression model. Secondly, a random-effect meta-regression model was performed to evaluate the annual variation in the $TV_{0–7}$ effect at the national level. The year variables and prefecture-year-specific coefficients of TV were set as the independent and dependent variable, respectively (Zhao et al., 2019).

2.3.4. *Sensitivity analysis*

Sensitivity analyses were performed to test the robustness of the results. Specifically, we changed the *dfs* for time trend (5–10) and RH (2–7) as well as the maximum lag (10–25). In addition, to examine whether the results were influenced by one prefecture, we obtained the pooled effect estimates after the exclusion of the prefecture. These tests were carried out using all-cause mortality alone.

All statistical analyses were performed using the R software (v.3.3.2). The "dlnm" package was used to establish the distributed lag non-linear model (Gasparrini et al., 2015b), and the "metafor" package was used to perform a meta-analysis (Gasparrini et al., 2012). The statistical significance was set at 0.05 level.

3. Results

A total of 39,941,731 deaths were recorded in 47 prefectures during our study period from 1972 to 2015. Fig. A2 shows the geographical locations of the 47 prefectures and their corresponding mean values of TV at 0–7 days of exposure. Total area by prefecture varies from 1876.8 km^2 (Kagawa) to 83,423.8 km^2 (Hokkaido) (http://www.gsi.go.jp/index.html). Table 1 shows the prefecture-specific characteristics according to daily all-cause mortality, mean temperature, and TV (preceding up to 7 days of exposure). The mean daily all-cause mortality ranged from 15 in Tottori to 211 in Tokyo. The daily mean temperature ranged from 8.9 °C in Hokkaido to 22.9 °C in Okinawa. TV had a similar pattern across the prefectures. Table A2 shows the descriptive statistics on cause-specific mortality for the 47 prefectures. Among the causes of death, the most common was circulatory disease, which accounted for 34.1% of all-cause mortality (6.6% from IHD, 15.2% from cerebrovascular disease, 5% from cerebral hemorrhage, and 6.1% from cerebral infarction), followed by respiratory disease, which accounted for 12.6% of deaths (7.9% from pneumonia, 0.5% from asthma, and 1.1% from COPD) (Table A3).

Fig. 1 depicts the effects of TV on all-cause mortality in each prefecture and the pooled mortality risk of TV at the national level in Japan. In most prefectures, the associations between TV and all-cause mortality were significant. In general, the estimates of all-cause mortality risk increased with longer exposure days with a few exceptions. The relationships between TV and cause-specific mortality as well as the pooled results are summarized in Figs. A3–A13.

Table 2 shows the pooled percent increase in cause-specific mortality associated with 1 °C increase in TV at different exposure days. I^2 statistics indicates a significant between-prefecture heterogeneity for TV at different exposure days (for example, $I^2 = 31.33\%$, $P = 0.02$; $I^2 = 46.83\%$, $P < 0.01$; $I^2 = 36.74\%$, $P < 0.01$ for TV at 0–1, 0–4 and 0–7 days of exposure, respectively). A 1 °C increase in TV at 0–1, 0–4, and 0–7 days of exposure was associated with 0.32% (95% confidence intervals (CI): 0.27%–0.36%), 0.77% (95% CI: 0.7%–0.84%) and 0.9% (95% CI: 0.82%–0.98%) increases in all-cause mortality, respectively.

Table 3
Estimated percent change (mean and 95% CI[a]) in the association between temperature variability and mortality per IQR[a] increase in prefecture-level predictors in Japan during 1972–2015. Data on unemployment (%), population, population density (people per km^2), GDP (Million JPY) and elderly (%) were collected from Census of Japan in 2012.

Variable	Percentage increase in mortality effect of temperature variability per IQR increase in prefecture variable			Heterogeneity parameter (τ^2)	Percentage of total variance due to between-study variance (%)
	IQR	Estimate (95% CI[a])	P-value		
Unemployment (%)	1.55	−0.05 (−0.16,0.06)	0.351	0.000003	0
Longitude	6.3	0.04 (−0.09,0.18)	0.536	0.000003	0
Latitude	2.3	−0.03 (−0.11,0.04)	0.346	0.000002	4.117901
Population	1598	0.03 (−0.01,0.07)	0.180	0.000002	7.863965
GDP (million JPY)	6,538,371.5	0.02 (0.00,0.05)	0.084	0.000002	15.996342
Elderly (%)	3.1	−0.09 (−0.20,0.02)	0.108	0.000002	13.754341
Population density (people per km^2)	297	0.02 (0.00,0.03)	0.042	0.000002	24.794018
Temperature (°C)	2.15	0.05 (−0.02,0.13)	0.158	0.000002	13.496877
Diurnal temperature (°C)	1.50	0.07 (−0.05,0.20)	0.226	0.000003	0
Relative humidity (%)	6.25	−0.19 (−0.31,−0.06)	0.003	0.000001	46.854258

[a] IQR, inter-quartile range; CI, confidence intervals.

Table 4
Joint modification of season and relative humidity level on mortality risk of temperature variability (TV) on all-cause mortality in Japan for per 1 °C increase in TV at different exposure days.

Exposure days	Warm & humid day	Warm & dry day	Cold & humid day	Cold & dry day
0–1 days	0.50 (0.45,0.56)	0.43 (0.39,0.48)	0.21 (0.16,0.26)	0.23 (0.18,0.27)
0–2 days	0.72 (0.65,0.78)	0.63 (0.57,0.69)	0.40 (0.33,0.46)	0.41 (0.35,0.46)
0–3 days	0.86 (0.78,0.93)	0.77 (0.71,0.83)	0.53 (0.45,0.60)	0.53 (0.47,0.60)
0–4 days	0.98 (0.90,1.06)	0.89 (0.83,0.96)	0.65 (0.57,0.73)	0.65 (0.58,0.72)
0–5 days	1.06 (0.98,1.14)	0.97 (0.9,1.04)	0.74 (0.65,0.82)	0.73 (0.65,0.81)
0–6 days	1.08 (1.00,1.16)	1.00 (0.92,1.07)	0.75 (0.67,0.84)	0.74 (0.67,0.82)
0–7 days	1.11 (1.02,1.19)	1.03 (0.95,1.10)	0.78 (0.69,0.86)	0.77 (0.68,0.85)

Based on the Q-AIC value, TV at 0–7 days of exposure was considered as the best fit (Table A4). At $TV_{0–7}$, the highest estimate was for asthma at 1.83% (95% CI: 1.07%–2.6%), followed by senility at 1.82% (95% CI: 1.49%–2.16%) and cerebral infarction at 1.39% (95%CI, 1.16–1.61%).

Fig. 2 illustrates the effects of per 1 °C increase in TV on cause-specific mortality at different exposure days. At the national level, for different exposure days from 0–1 to 0–7 days, generally the similar patterns-increased along with exposure days and plateaued after $TV_{0–5}$- were found in the effects of TV on different mortality types. The effects of TV peaked at 0–7 exposure days with the exception of renal disease, cerebral hemorrhage, and COPD.

Table 3 shows the results of the modification effect by 10 prefecture-level factors. Individuals in the prefectures with high population density and low RH were more vulnerable to the impacts of TV. Approximately 24.8% and 46.9% of the total heterogeneity can be attributed to these two factors, respectively. However, other prefecture-level factors showed no significant effect modification. Further analysis estimated the mortality risk of TV by four combinations of season and RH level. We consistently found TV had significantly higher mortality risks on warm and humid days over different exposure days. For example, on warm and humid days, a 1 °C increase in TV at 0–7 days of exposure was associated with an increase of 1.11% (95% CI: 1.02%–1.19%) for all-cause mortality, while on other days, much lower effects were observed (Table 4).

Fig. 3 displays the annual change in the coefficient of TV effect at 0–7 days of exposure during 1972–2015. Nationally, there was a significant declining trend in the effect estimates of $TV_{0–7}$ on all-cause mortality, with a yearly change of −0.000096 (95% confidence intervals: −0.000156, −0.000036, $P < 0.01$). Furthermore, we found decreasing trends in annual mean $TV_{0–7}$ in most prefectures, and the annual mean $TV_{0–7}$ decreased significantly with a rate of 0.005 °C per year at the national scale during our study period ($P < 0.01$) (Fig. A14).

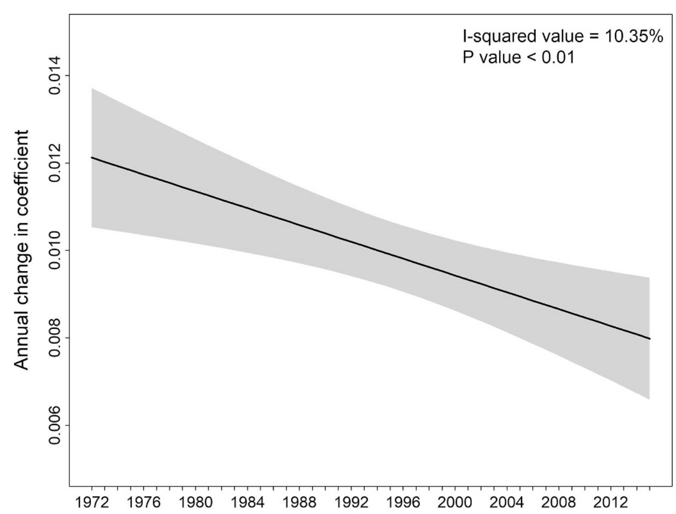

Fig. 3. The annual change in coefficient of the association between temperature variability and all-cause mortality at 0–7 days of exposure in Japan during 1972–2015.

To check the robustness of our results, we performed sensitivity analyzes by changing modeling strategies. We changed *dfs* for time trend (5–10) and RH (2–7), and lag for temperature (10–25). The results were similar among the different modeling strategies (Fig. A15). We also obtained the pooled effect estimates after excluding one prefecture each time to test whether our main findings were influenced by the prefecture and found there was no big difference (Fig. A16).

4. Discussion

To the best of our knowledge, this is the largest study that comprehensively quantified the relationship between TV and cause-specific mortality both regionally and nationally in Japan. We found that the effects of TV varied across prefectures. However, at the national scale, TV was significantly associated with all-cause and cause-specific mortality. Moreover, we consistently observed that mortality risk due to TV increased with longer exposure days. Among the 11 causes of death, TV had a higher mortality risk for asthma and senility than others. Further analysis showed evidence for enhanced mortality risk due to TV in densely populated areas and on warm and humid days. Our findings may contribute to public health decision-making in repose to climate change.

Numerous ecological studies have shown that TV has detrimental impacts on human health (Yang et al., 2013; Cheng et al., 2014b; Vicedo-Cabrera et al., 2016). Among the comparable results, for example, a study conducted in east Asia, which involved six Japanese prefectures (Hokkaido, Miyagi, Tokyo, Aichi, Osaka, and Fukuoka) (Kim et al., 2016), showed that per 1 °C increase in intra-day TV was associated with 0.39% (95% CI: −0.08%–0.85%), 0.38% (95% CI: 0.26%–1.02%), 0.90% (95% CI: 0.70%–1.11%), 0.92% (95% CI: 0.56%–1.28%), 0.44% (95% CI: 0.13%–0.75%), and 0.17% (95% CI: −0.29%–0.63%) change in all-cause mortality in six prefectures, respectively. Based on a new index for TV, the present study observed a larger estimate for mortality risk associated with per 1 °C increase in TV in each of the six prefectures. Since TV consists of two components, i.e., intra- and inter-day variations in temperature, those studies that only considered one of two components may not fully capture the magnitudes of TV impacts. In contrast, up to this point, only six studies have considered both intra- and inter-day TV when assessing the mortality or morbidity risk of TV (Guo et al., 2016; Cheng et al., 2017; Zhang et al., 2017; Yang et al., 2018; Zhao et al., 2018; Hu et al., 2019). One of the abovementioned studies has shown a significant association between TV and mortality at a national scale in Japan (Guo et al., 2016). Although the estimated size of the overall effects of TV is alike, the lag pattern is slightly different. Our result showed that the effects of TV plateaued after $TV_{0–5}$. We speculate the possible reason is the smaller number of deaths and/or the shorter study period in their study. In addition, their study did not investigate the associations between TV and various causes of death in Japan, and this issue must be assessed.

In the present study, the overall estimate of the effects of TV consistently increased along with the exposure days, and it was most pronounced at 0–6 or 0–7 days of exposure in Japan (except for cerebral hemorrhage). Although this result was in accordance with that of a recent study conducted in the same population (Guo et al., 2016), the lag patterns of association between TV and mortality differed from those of previous studies conducted in Australia (Zhao et al., 2018) and China (Zhang et al., 2017; Hu et al., 2019), where shorter exposure to TV was more detrimental and lag patterns among cause-specific mortality were inconsistent. The discrepancy might be attributed to the different population size, local climatic adaptation, and effect modification by city-specific characteristics (Guo et al., 2016; Zhao et al., 2018). More studies must be conducted to comprehensively evaluate the lag patterns of the association between TV and mortality in different climatic zones.

As with all-cause mortality, we observed that TV was also strongly associated with several types of cause-specific mortality. Although the underlying mechanisms are unclear, substantial evidence based on physiology, immunology, and behavior science has shown that a sudden temperature change was related to a higher mortality risk (Vicedo-Cabrera et al., 2016; Ban et al., 2017; Cheng et al., 2017). A possible explanation is that a marked variation in ambient temperature is associated with changes in heart rate, systolic and diastolic blood pressure, oxygen uptake, mucociliary clearance and leukocyte phagocytosis, and impairment in thermoregulatory capacity, which may trigger circulatory- and respiratory-related diseases (Medina-Ramón and Schwartz, 2007; O'neill and Ebi, 2009; Lim et al., 2012; Yang et al., 2013; Cheng et al., 2014a; Lim et al., 2015). The present study also confirmed the strong associations between TV and circulatory-, and respiratory-related mortality. However, the finding is inconclusive due to the inconsistent results of the studies, including non-epidemiological studies, and such results must be validated. For example, some studies have not shown that TV has significant effects on respiratory and IHD mortality (Cheng et al., 2017; Zhang et al., 2017). This result might be partly explained by the small number of daily death tolls in their study (Zhang et al., 2017). In addition to circulatory- and respiratory-related mortality, the present study also found the strong association between TV and mortality from renal disease and senility. The underlying rationales related to the increase in renal deaths with temperature variation have been postulated. A dramatic increase in temperature above threshold can cause hyperthermia and hydration. When body's biological mechanisms attempt to regulate water and electrolyte imbalance, glomerular filtration rates decrease, which may cause renal failure (Hansen et al., 2008b). To date, few studies have investigated TV-aggravated mortality due to senility. However, evidence has shown that fluctuations in temperature were related to an increase in hospital admissions for senility (Hansen et al., 2008a). A plausible explanation for TV-related mortality from senility is that rapid temperature changes may accelerate mental infirmity and physical deterioration in the elderly, especially for those with pre-existing chronic diseases (Hansen et al., 2008a; Kenny et al., 2010). Considering the large proportion of the elderly population in Japan, future studies are needed to validate this finding and provide implications for improving the quality of geriatric care.

We found a higher mortality risk for individuals living in densely populated areas. This finding was similar to that of previous studies (Medina-Ramón and Schwartz, 2007; Ma et al., 2015; Yang et al., 2018). Although the rationale behind the role of population density in the association between TV and mortality is still debated (Cheng et al., 2017), it can be partly explained by the phenomenon that a high population density results in higher temperatures through urban heat land effect particularly in summer, which poses a greater risk to health particularly in elderly individuals (Medina-Ramón and Schwartz, 2007; Tomlinson et al., 2011). Therefore, more efforts should be exerted in better urban planning particularly for an aging society like Japan. In addition, we found regions with a high RH level can ameliorate the mortality risk due to TV, which was inconsistent with some previous studies (Ma et al., 2015; Yang et al., 2018; Zhang et al., 2018). This discrepancy may be attributed to the long-term biological adaptation to local weather conditions (Zhang et al., 2018), which was also confirmed in our further analysis of joint effect modifications of season and RH on TV-mortality associations. Significant higher mortality risk of TV was observed on warm and humid days than other days, suggesting that people living in areas with low RH might not adapt efficiently to the sudden increase in RH. Regarding the joint role of season and humidity, a plausible explanation is that hot suffocating weather with high humidity can cause body to overheat, impede its ability to regulate body temperature and cool down (Basu, 2009).

Nationally, we observed a significant decline in vulnerability to TV-related mortality during the 44-year study period. This may relate to the physiological adaptation to extreme temperatures (Gasparrini et al., 2015a), economic development, urbanization, and health care improvement (e.g. increased access to air conditioning) (Kovats and Hajat, 2008). However, this finding was not consistent in different regions. A recent Brazilian study showed a long-term rise in morbidity risk of TV despite its dramatic economic growth and significant improvement in public health services (Zhao et al., 2018). More research is thus needed to identity the exact drivers of the observed temporal variation in this study. Furthermore, we detected a decreasing trend of annual mean TV in most prefectures during 1972–2015, which could be associated with some factors, such as land use change, aerosols and greenhouse emissions. Although the decreasing TV in future climate scenarios might bring health benefits, the net change in excess mortality needs to be evaluated after accounting for the change in heat- and cold-mortality relationships.

In the present study, we adopted a newly proposed TV index that can account for both intra- and inter-day TV and conducted a time-series analysis by using a national big data set to assess the impact of TV on mortality. Therefore, our work may have some practical implications. First, our findings would contribute to deepening the understanding of the complex associations between TV and mortality. Second, public health officials and specialists in all relevant domains should work together to establish an early warning system to inform and alert citizens of impending rapid temperature changes and provide necessary aids to minimize losses due to temperature variation, particularly in the vulnerable groups.

Some limitations of the present study should be acknowledged. First, the TV index in this study may be inconvenient to interpret because of the use of the relative scale, which may hinder its application to developing guidance for the health protection. For example, although our findings indicated an urgent need to reduce TV-related mortality, without offering information on the direction of temperature change, we may fail to tell whether the mortality risk is more from significant temperature drop or great temperature increase. Thus, more studies regarding this issue are warranted to help to improve this indicator. Second, although we used the largest meteorological and mortality time-series data set of Japan, we only used one-year (2012) prefecture-level data due to the lack of the relevant prefecture-specific data, which may result in the lack of preciseness when quantifying the effect modifications. Third, we did not stratify the statistical analyses according to individual factors, such as age, gender, and education level, which may mask vulnerabilities for specific sub-groups. But most likely, the elderly, female and those with low educational level are the most sensitive to TV. Fourth, we did not have information on individual exposure, which may cause measurement errors. More evidence is needed to confirm this issue using different study designs. Fifth, the weather data were collected from only one monitoring station for each prefecture, which may lead to exposure misclassification due to intra-prefecture variability in climate conditions. Sixth, we did not include air pollutants in the analysis. However, previous studies have shown that air pollutants did not modify the associations between TV and mortality (Lim et al., 2012; Guo et al., 2016).

5. Conclusions

Our study strengthened the evidence that TV was an independent risk factor for several causes of death particularly in those with asthma and senility. In addition, consistent lag patterns were observed, which showed that the effects of TV increased with longer exposure days with some differences depending on the cause of death. TV-related mortality may increase in densely populated areas and on warm and humid days. Public health strategies that aim to prevent and minimize TV-related mortality are strongly recommended.

Author contributions

C.M. initiated this study. C.M. and J.Y. performed statistical analysis. Y.H. acquired data. C.M. drafted the manuscript. J.Y., S.F.N. and Y.H. revised the manuscript. All authors approved the final manuscript.

Ethics committee approval

Ethical approval was not required for secondary analysis of anonymous data in this study.

Acknowledgements

This research was supported by the Environment Research and Technology Development Fund (S-14) of the Environmental Restoration and Conservation Agency of Japan. J.Y. was supported by the Natural Science Foundation of Guangdong Province of China (No. 2018A030310655) and the Science and Technology Planning Project of Guangdong Province of China (2014B090901058).

Conflict of interests

The authors declare they have no actual or potential competing financial interests.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2019.03.025.

References

Ban, J., Xu, D., He, M.Z., Sun, Q., Chen, C., Wang, W., Zhu, P., Li, T., 2017. The effect of high temperature on cause-specific mortality: a multi-county analysis in China. Environ. Int. 106, 19–26.

Basu, R., 2009. High ambient temperature and mortality: a review of epidemiologic studies from 2001 to 2008. Environ. Health 8 (1), 40.

Bathiany, S., Dakos, V., Scheffer, M., Lenton, T.M., 2018. Climate models predict increasing temperature variability in poor countries. Sci. Adv. 4 (5), eaar5809.

Bhaskaran, K., Gasparrini, A., Hajat, S., Smeeth, L., Armstrong, B., 2013. Time series regression studies in environmental epidemiology. Int. J. Epidemiol. 42 (4), 1187–1195.

Cheng, J., Xu, Z., Zhu, R., Wang, X., Jin, L., Song, J., Su, H., 2014a. Impact of diurnal temperature range on human health: a systematic review. Int. J. Biometeorol. 58 (9), 2011–2024.

Cheng, J., Zhu, R., Xu, Z., Xu, X., Wang, X., Li, K., Su, H., 2014b. Temperature variation between neighboring days and mortality: a distributed lag non-linear analysis. International Journal of Public Health 59 (6), 923–931.

Cheng, J., Xu, Z., Bambrick, H., Su, H., Tong, S., Hu, W., 2017. The mortality burden of hourly temperature variability in five capital cities, Australia: time-series and meta-regression analysis. Environ. Int. 109, 10–19.

Gasparrini, A., Armstrong, B., Kenward, M., 2012. Multivariate meta-analysis for non-linear and other multi-parameter associations. Stat. Med. 31 (29), 3821–3839.

Gasparrini, A., Guo, Y., Hashizume, M., Kinney, P.L., Petkova, E.P., Lavigne, E., Zanobetti, A., Schwartz, J.D., Tobias, A., Leone, M., 2015a. Temporal variation in heat–mortality associations: a multicountry study. Environ. Health Perspect. 123 (11), 1200.

Gasparrini, A., Guo, Y., Hashizume, M., Lavigne, E., Zanobetti, A., Schwartz, J., Tobias, A., Tong, S., Rocklöv, J., Forsberg, B., 2015b. Mortality risk attributable to high and low ambient temperature: a multicountry observational study. Lancet 386 (9991), 369–375.

Guo, Y., Gasparrini, A., Armstrong, B., Li, S., Tawatsupa, B., Tobias, A., Lavigne, E., Coelho, M.d.S.Z.S., Leone, M., Pan, X., 2014. Global variation in the effects of ambient temperature on mortality: a systematic evaluation. Epidemiology (Cambridge, Mass.) 25 (6), 781.

Guo, Y., Gasparrini, A., Armstrong, B.G., Tawatsupa, B., Tobias, A., Lavigne, E., Coelho, M.d.S.Z.S., Pan, X., Kim, H., Hashizume, M., 2016. Temperature variability and mortality: a multi-country study. Environ. Health Perspect. 124 (10), 1554.

Hajat, S., Vardoulakis, S., Heaviside, C., Eggen, B., 2014. Climate change effects on human health: projections of temperature-related mortality for the UK during the 2020s, 2050s and 2080s. J. Epidemiol. Community Health 68 (7), 641–648.

Hansen, A., Bi, P., Nitschke, M., Ryan, P., Pisaniello, D., Tucker, G., 2008a. The effect of heat waves on mental health in a temperate Australian city. Environ. Health Perspect. 116 (10), 1369–1375.

Hansen, A.L., Bi, P., Ryan, P., Nitschke, M., Pisaniello, D., Tucker, G., 2008b. The effect of heat waves on hospital admissions for renal disease in a temperate city of Australia. Int. J. Epidemiol. 37 (6), 1359–1365.

Hu, K., Guo, Y., Yang, X., Zhong, J., Fei, F., Chen, F., Zhao, Q., Zhang, Y., Chen, G., Chen, Q., 2019. Temperature variability and mortality in rural and urban areas in Zhejiang province, China: an application of a spatiotemporal index. Sci. Total Environ. 647, 1044–1051.

Huang, C., Barnett, A.G., Xu, Z., Chu, C., Wang, X., Turner, L.R., Tong, S., 2013. Managing the health effects of temperature in response to climate change: challenges ahead. Environ. Health Perspect. 121 (4), 415.

IPCC, 2014. Climate Change 2014: Synthesis Report.

Kenny, G.P., Yardley, J., Brown, C., Sigal, R.J., Jay, O., 2010. Heat stress in older individuals and patients with common chronic diseases. Can. Med. Assoc. J. 182 (10), 1053–1060.

Kim, J., Shin, J., Lim, Y.-H., Honda, Y., Hashizume, M., Guo, Y.L., Kan, H., Yi, S., Kim, H., 2016. Comprehensive approach to understand the association between diurnal temperature range and mortality in East Asia. Sci. Total Environ. 539, 313–321.

Kovats, R.S., Hajat, S., 2008. Heat stress and public health: a critical review. Annu. Rev. Public Health 29, 41–55.
Lim, Y.-H., Hong, Y.-C., Kim, H., 2012. Effects of diurnal temperature range on cardiovascular and respiratory hospital admissions in Korea. Sci. Total Environ. 417, 55–60.
Lim, Y.-H., Reid, C.E., Mann, J.K., Jerrett, M., Kim, H., 2015. Diurnal temperature range and short-term mortality in large US communities. Int. J. Biometeorol. 59 (9), 1311–1319.
Lin, H., Zhang, Y., Xu, Y., Xu, X., Liu, T., Luo, Y., Xiao, J., Wu, W., Ma, W., 2013. Temperature changes between neighboring days and mortality in summer: a distributed lag non-linear time series analysis. PLoS One 8 (6), e66403.
Ma, W., Chen, R., Kan, H., 2014. Temperature-related mortality in 17 large Chinese cities: how heat and cold affect mortality in China. Environ. Res. 134, 127–133.
Ma, W., Zeng, W., Zhou, M., Wang, L., Rutherford, S., Lin, H., Liu, T., Zhang, Y., Xiao, J., Zhang, Y., 2015. The short-term effect of heat waves on mortality and its modifiers in China: an analysis from 66 communities. Environ. Int. 75, 103–109.
Medina-Ramón, M., Schwartz, J., 2007. Temperature, temperature extremes, and mortality: a study of acclimatization and effect modification in 50 United States cities. Occup. Environ. Med. 64 (12), 827–833.
O'neill, M.S., Ebi, K.L., 2009. Temperature extremes and health: impacts of climate variability and change in the United States. J. Occup. Environ. Med. 51 (1), 13–25.
Portal Site of Official Statistics of Japan, 2017. Vital statistics of Japan. https://www.e-stat.go.jp/en/stat-search/files?page=1&layout=datalist&toukei=00450011&tstat=000001028897&cycle=7&year=20160&month=0&tclass1=000001053058&tclass2=000001053061&tclass3=000001053065&result_back=1&second=1&second2=1.
Sakamitsu, K., 2018. Vital Statistics in Japan-Trends up to 2016. Ministry of Health, Labor and Welfare of Japan. https://www.mhlw.go.jp/english/database/db-hw/dl/81-1a2en.pdf.
Schär, C., Vidale, P.L., Lüthi, D., Frei, C., Häberli, C., Liniger, M.A., Appenzeller, C., 2004. The role of increasing temperature variability in European summer heatwaves. Nature 427 (6972), 332.
Thomas, F., Sabel, C.E., Morton, K., Hiscock, R., Depledge, M.H., 2014. Extended impacts of climate change on health and wellbeing. Environ. Sci. Pol. 44, 271–278.
Tomlinson, C.J., Chapman, L., Thornes, J.E., Baker, C.J., 2011. Including the urban heat island in spatial heat health risk assessment strategies: a case study for Birmingham, UK. Int. J. Health Geogr. 10 (1), 42.
Vardoulakis, S., Dear, K., Hajat, S., Heaviside, C., Eggen, B., McMichael, A.J., 2014. Comparative assessment of the effects of climate change on heat-and cold-related mortality in the United Kingdom and Australia. Environ. Health Perspect. 122 (12), 1285.
Vicedo-Cabrera, A.M., Forsberg, B., Tobias, A., Zanobetti, A., Schwartz, J., Armstrong, B., Gasparrini, A., 2016. Associations of inter-and intraday temperature change with mortality. Am. J. Epidemiol. 183 (4), 286–293.
Viechtbauer, W., 2010. Conducting meta-analyses in R with the metafor package. J. Stat. Softw. 36 (3).
Yang, J., Ou, C.-Q., Ding, Y., Zhou, Y.-X., Chen, P.-Y., 2012. Daily temperature and mortality: a study of distributed lag non-linear effect and effect modification in Guangzhou. Environ. Health 11 (1), 63.
Yang, J., Liu, H.-Z., Ou, C.-Q., Lin, G.-Z., Zhou, Q., Shen, G.-C., Chen, P.-Y., Guo, Y., 2013. Global climate change: impact of diurnal temperature range on mortality in Guangzhou, China. Environ. Pollut. 175, 131–136.
Yang, J., Zhou, M., Li, M., Liu, X., Yin, P., Sun, Q., Wang, J., Wu, H., Wang, B., Liu, Q., 2018. Vulnerability to the impact of temperature variability on mortality in 31 major Chinese cities. Environ. Pollut. 239, 631–637.
Yi, W., Chan, A.P., 2015. Effects of temperature on mortality in Hong Kong: a time series analysis. Int. J. Biometeorol. 59 (7), 927–936.
Zhang, Y., Yu, C., Bao, J., Li, X., 2017. Impact of temperature variation on mortality: an observational study from 12 counties across Hubei Province in China. Sci. Total Environ. 587, 196–203.
Zhang, Y., Peng, M., Wang, L., Yu, C., 2018. Association of diurnal temperature range with daily mortality in England and wales: a nationwide time-series study. Sci. Total Environ. 619, 291–300.
Zhao, Q., Coelho, M.S., Li, S., Saldiva, P.H., Hu, K., Abramson, M.J., Huxley, R.R., Guo, Y., 2018. Spatiotemporal and demographic variation in the association between temperature variability and hospitalizations in Brazil during 2000–2015: a nationwide time-series study. Environ. Int. 120, 345–353.
Zhao, Q., Li, S., Coelho, M.S., Saldiva, P.H., Hu, K., Arblaster, J.M., Nicholls, N., Huxley, R.R., Abramson, M.J., Guo, Y., 2019. Geographic, demographic, and temporal variations in the association between heat exposure and hospitalization in Brazil: a nationwide study between 2000 and 2015. Environ. Health Perspect. 127 (01), 017001.