Science of the Total Environment 682 (2019) 333–339

Contents lists available at ScienceDirect

Science of the Total Environment

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

Future projections of temperature-related excess out-of-hospital cardiac arrest under climate change scenarios in Japan

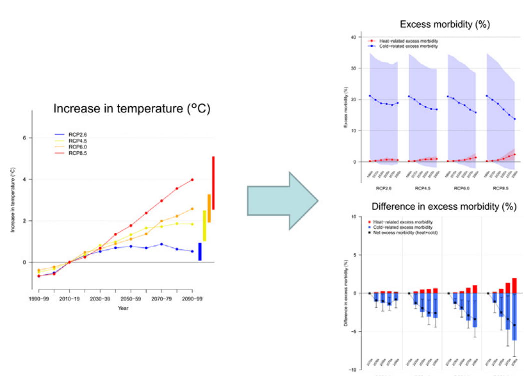
Daisuke Onozuka [a,b,*], Antonio Gasparrini [c,d], Francesco Sera [c], Masahiro Hashizume [e], Yasushi Honda [f]

[a] *Department of Preventive Medicine and Epidemiologic Informatics, National Cerebral and Cardiovascular Center Research Institute, Osaka, Japan*
[b] *Department of Health Communication, Kyushu University Graduate School of Medical Sciences, Fukuoka, Japan*
[c] *Department of Public Health, Environments and Society, London School of Hygiene & Tropical Medicine, London, UK*
[d] *Centre for Statistical Methodology, London School of Hygiene & Tropical Medicine, London, UK*
[e] *Department of Pediatric Infectious Diseases, Institute of Tropical Medicine, Nagasaki University, Nagasaki, Japan*
[f] *Faculty of Health and Sport Sciences, University of Tsukuba, Tsukuba, Japan*

HIGHLIGHTS

- We projected temperature-related morbidity for OHCA under climate change scenarios.
- Japan is projected to have a net reduction in OHCA in higher-emission scenarios.
- A broader assessment of climate change-related CVD morbidity should be considered.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 8 February 2019
Received in revised form 29 April 2019
Accepted 14 May 2019
Available online 16 May 2019

Editor: SCOTT SHERIDAN

Keywords:
Cardiac arrest
Climate change
Excess morbidity
Sudden death
Temperature

ABSTRACT

Background: Recent studies have reported associations between global climate change and mortality. However, future projections of temperature-related out-of-hospital cardiac arrest (OHCA) have not been thoroughly evaluated. Thus, we aimed to project temperature-related morbidity for OHCA concomitant with climate change.
Methods: We collected national registry data on all OHCA cases reported in 2005–2015 from all 47 Japanese prefectures. We used a two-stage time series analysis to estimate temperature-OHCA relationships. Time series of current and future daily mean temperature variations were constructed according to four climate change scenarios of representative concentration pathways (RCPs) using five general circulation models. We projected excess morbidity for heat and cold and the net change in 1990–2099 for each climate change scenario using the assumption of no adaptation or population changes.
Results: During the study period, 739,717 OHCAs of presumed cardiac origin were reported. Net decreases in temperature-related excess morbidity were observed under higher emission scenarios. The net change in 2090–2099 compared with 2010–2019 was −0.8% (95% empirical confidence interval [eCI]: −1.9, 0.1) for a mild emission scenario (RCP2.6), −2.6% (95% eCI: −4.4, −0.8) for a stabilization scenario (RCP4.5), −3.4% (95% eCI: −5.7, −1.0) for a stabilization scenario (RCP6.0), and − 4.2% (95% eCI: −8.3, −0.1) for an extreme emission scenario (RCP8.5).

* Corresponding author at: Department of Preventive Medicine and Epidemiologic Informatics, National Cerebral and Cardiovascular Center Research Institute, 5-7-1 Fujishirodai, Suita, Osaka 565-8565, Japan.
E-mail address: onozukad@ncvc.go.jp (D. Onozuka).

https://doi.org/10.1016/j.scitotenv.2019.05.196

Conclusions: Our study indicates that Japan is projected to experience a substantial net reduction in OHCAs in higher-emission scenarios. The decrease in risk is limited to a specific morbidity cause, and a broader assessment within climate change scenarios should consider other direct and indirect impacts.

1. Introduction

Climate change is widely recognized as the most significant global health threat of the 21st century, and tackling climate change could be the greatest global health opportunity (Watts et al., 2015). The fifth Intergovernmental Panel on Climate Change (IPCC) report indicates that high-end emissions scenarios project increases in global mean temperatures of between 2.6 and 4.8 °C by the end of the century (Pachauri et al., 2014). While a number of important human diseases have been associated with shifts in climate, a lack of long-term, high-quality data and a significant influence from socio-economic factors has led to some uncertainty in attributing any increase or re-emergence of diseases to climate change (Patz et al., 2005). Recent studies have shown that climate change has the potential to substantially increase temperature-related mortality (Benmarhnia et al., 2014; Gasparrini et al., 2017; Hajat et al., 2014; Lee and Kim, 2016). However, the future impact of health threats arising from climate change can differ quite significantly among diseases (Watts et al., 2015), and the impacts of climate change on morbidity has not been thoroughly evaluated.

Sudden cardiac arrest is a major contributor to morbidity and mortality in the general population, and accounts for almost 10–20% of all deaths (Field et al., 2010). In particular, out-of-hospital cardiac arrest (OHCA) is characterized by unexpected collapse due to a cardiac disorder (Tian and Qiu, 2017). Although resuscitation rates are generally improving globally, OHCA is a leading global cause of mortality (Nichol et al., 2008; Wissenberg et al., 2013). Coronary artery disease is a key contributor to sudden cardiac arrest (Mozaffarian et al., 2015). However, OHCA is multifactorial and complex in nature (Patz et al., 2005). Several studies that aimed to quantify the burden of OHCA have had difficulty accurately accounting for potential adaptation to climate change over time and place. Meanwhile, OHCA remains a prime and significant cause of death due to cardiovascular diseases. It is therefore paramount to focus on OHCA to improve prediction estimates and to aid in prioritizing mitigation and adaptation policies to climate change in the future.

As concerns associated with climate change have increased over the past few decades, there has been emerging evidence supporting a relationship between OHCA and environmental factors such as extreme weather conditions like heat and cold events (Onozuka and Hagihara, 2017a, c, e). For example, several studies have shown a positive association between extremely high and low temperatures and OHCA risk (Onozuka and Hagihara, 2017a). Moreover, recent studies have also shown that the majority of temperature-related OHCA burden is attributable to low temperatures, and that the effect of extreme temperatures is substantially lower than that of moderate temperatures (Onozuka and Hagihara, 2017c). These findings suggest that climate change may raise heat-related morbidity, while concomitantly reducing cold-related morbidity. However, future projections of temperature-related excess morbidity due to OHCA according to climate change scenarios have not been studied. Furthermore, the degree to which the anticipated reduction in cold-related morbidity can counter the rise in heat-related morbidity remains to be determined. This data will be important for the development of coordinated and evidence-based climate change and public health methods to prevent climate change-related OHCA.

Here, we aimed to project the future impact of climate change on temperature-attributable OHCA morbidity using Japanese national registry data from all OHCA cases reported in 2005–2015 that were assumed to be of cardiac origin.

2. Methods

2.1. Study design

We used the same study design and statistical framework described in detail elsewhere (Gasparrini et al., 2017; Vicedo-Cabrera et al., 2019). Briefly, we used a two-stage time-series analysis to predict the association between temperature and daily morbidity due to OHCA in all 47 Japanese prefectures. Additionally, we acquired daily mean temperature time-series according to climate change scenarios of the four representative concentration pathways (RCPs), RCP2.6, RCP4.5, RCP6.0, and RCP8.5. We merged these data to estimate future projections of excess morbidity attributable to temperature.

2.2. Ethics approval

This study was approved by the Ethics Committee of the Kyushu University Graduate School of Medical Sciences. Written informed consent was not required because of the retrospective observational nature of this study, which used national registry data, and the fact that enrolled subjects were deidentified by the Fire and Disaster Management Agency (FDMA).

2.3. Data sources

We used national registry data from the FDMA regarding all OHCA cases that were reported from 2005 to 2015 in all 47 Japanese prefectures. According to Japan's Fire Service Act, municipal government-enlisted emergency medical services (EMSs) are provided at around 800 fire stations and related dispatch centers across Japan. Given that EMS providers do not have the authority to terminate resuscitation in the field, all EMS-treated OHCA cases are transported to a hospital. EMS personnel summarize each OHCA case in conjunction with the physician in charge according to the standardized Utstein-style reporting guidelines for cardiac arrest (Hagihara et al., 2012). The physician in charge together with the EMS personnel clinically ascertained the cause of cardiac arrest (i.e., presumed cardiac or non-cardiac). All arrests were considered to be of cardiac origin unless the cause was drowning, trauma, drug overdose, exsanguination, asphyxia, or any other obvious non-cardiac cause. Fire stations with dispatch centers in the 47 prefectures send their data to the FDMA, where the data is incorporated into the national registry system on the FDMA database server. According to the Fire Service Act, all OHCA cases must be registered in Japan. The national registry data for OHCA cases is therefore regarded as comprehensive across the country. The FDMA's computer system was used to check and validate the data for consistency (Kitamura et al., 2016). We included all patients that experienced an OHCA of presumed cardiac origin, and we extracted the daily time-series of OHCA cases from the national registry database.

We also acquired data on daily mean temperatures from the Japan Meteorological Agency. Data from one weather station positioned in an urban area of the capital city was used as representative data for the region for each prefecture because these were synoptic climatological stations and intended to capture macro-scale weather for each prefecture. Daily mean temperatures were computed as 24-hour averages according to hourly measurements. Daily mean temperature was used as the main exposure index as it is indicative of exposure throughout the day and can be readily interpreted for decision-making purposes (Guo et al., 2011, 2014).

2.4. Scenario models

We estimated the projections of future temperature-related OHCA under four climate change scenarios using models of climate change and morbidity. First, we acquired time series data for daily mean temperatures according to four climate change scenarios of RCPs (van Vuuren et al., 2011a). The four RCPs (RCP2.6, RCP4.5, RCP6.0, and RCP8.5) present rising greenhouse gas concentration trajectories: RCP2.6 models a mild emission scenario in which peaks in radiative forcing at ~3 W/m^2 before 2100 and then declines to 2.6 W/m^2 by 2100, RCP4.5 models a stabilization scenario in which total radiative forcing is stabilized shortly after 2100, without overshooting the long-run radiative forcing target level of 4.5 W/m^2, RCP6.0 models a stabilization scenario in which total radiative forcing is stabilized shortly after 2100, without overshoot pathway to 6.0 W/m^2, by the application of a range of technologies and strategies for reducing greenhouse gas emissions, and RCP8.5 models an extreme emission scenario in which rising radiative forcing pathway leading to 8.5 W/m^2 by 2100 (van Vuuren et al., 2011a). The RCPs were generated following collaborations between integrated assessment modelers, climate modelers, terrestrial ecosystem modelers, and emission inventory experts (van Vuuren et al., 2011a). Future projections of daily mean temperatures under each RCP were then developed using general circulation models (GCMs) (Warszawski et al., 2014). GCMs were designed to enable the quantification of representation of historical, current, and projected climate consistent with scenarios of increases in radiative atmospheric forces, summarized by RCPs. The Inter-Sectoral Impact Model Intercomparison Project (ISI-MIP) database includes daily temperature series for each RCP scenario of five GCMs (GFDL-ESM2M (Dunne et al., 2012, 2013), HadGEM2-ES (Jones et al., 2011), IPSL-CM5A-LR (Mignot and Bony, 2013), MIROC-ESM-CHEM (Watanabe et al., 2011), and NorESMI-M (Bentsen et al., 2013; Iversen et al., 2013)), and these five GCMs were regarded as the representatives of the full range of projections of future climate based on the current existing scientific literature within the fifth phase of the Climate Model Intercomparison Project (CMIP5) models (Taylor et al., 2012; Warszawski et al., 2014). The ISI-MIP database (https://www.isimip.org/) contains time series of daily mean temperatures for historical (1960–2005) and projected (2006–2099) periods, which are bias-corrected and downscaled to $0.5° \times 0.5°$ spatial resolution (Warszawski et al., 2014). GCMs were generated by considering the difference in climate change impact at varying levels of global warming according to the four RCPs to produce the highest and lowest end-of-century forcings (Warszawski et al., 2014). When the modelled daily temperature series are applied to exposure-response relationships estimated using observed daily time series for daily mean temperature, deviations between the modelled and observed daily temperature series may produce biased results in the impact projections. Therefore, the modelled daily temperature series were corrected using the bias-correction method, which recalibrated using the monthly mean and the daily variability around the monthly mean of observed daily temperature series (Hempel et al., 2013). We calculated the projected daily time series of OHCAs as the mean observed count for each day of the year, and repeated this across the projection period (1990–2099).

2.5. Statistical analysis

2.5.1. Estimation of exposure-response relationships

We used two-stage time series analysis to predict the prefecture-specific non-linear lag impact of temperature on OHCA, as described previously (Gasparrini et al., 2016; Onozuka and Hagihara, 2017c; Zhang et al., 2019, 2017). Briefly, first, we investigated the association between temperature and OHCA in individual prefectures using a time-series quasi-Poisson regression model combined with a distributed lag non-linear model, adjusting for season, long-term trends, and day of the week. We examined lag periods of up to 21 days to consider the delayed impact of low temperatures. Second, we combined prefecture-specific estimates using multivariate meta-regression models to predict the nationwide non-linear temperature-OHCA association. This method has been described in detail elsewhere (Gasparrini et al., 2017; Vicedo-Cabrera et al., 2019).

2.5.2. Projection of the effect on morbidity

We projected excess morbidity due to temperature using the daily temperature and morbidity time-series model according to the assumption of no adaptation or population changes, as described previously (Gasparrini et al., 2016; Onozuka and Hagihara, 2017c). Briefly, we determined the minimum morbidity temperature using the lowest value of the total cumulative relative risk between temperature and OHCA. We used the minimum morbidity temperature as a reference to compute the attributable risk by re-centering the natural cubic spline. This value was regarded as the optimal temperature. The total attributable number of OHCAs as a result of non-optimal temperatures was computed as the sum of contributions from all days in the series. The ratio of this value to the total number of OHCAs was regarded as the total attributable fraction. Components that were attributable to low and high temperatures were computed by accumulating the subsets corresponding to days with temperatures below or above the minimum morbidity temperature. First, we estimated the excess morbidity for each prefecture and combinations of GCMs and RCPs. Second, we computed attributable fractions as GCM-ensemble means according to decade and RCP using the respective total number of OHCAs as the denominator. Monte Carlo simulations were used to compute empirical confidence intervals (eCIs), calculate the uncertainty in both the estimated exposure-lag-response association and climate projections among GCMs. Details of this method were described previously (Gasparrini et al., 2017; Vicedo-Cabrera et al., 2019).

For sensitivity analysis, modeling selections were tested by controlling for different degrees of freedom for time trends (6 and 10 degrees of freedom per year), by choosing different lags (14 and 28 days), and by including or excluding different confounding factors (relative humidity, public holiday, and day of the week). All statistical analyses were conducted using R 3.5.0 (R Core Team, R Foundation for Statistical Computing, Vienna, Austria), specifically using the *dlnm* and *mvmeta* packages.

3. Results

A total of 739,717 OHCA cases of presumed cardiac origin were registered between January 1, 2005 and December 31, 2015 in the 47 prefectures of Japan. The daily mean temperature was 15.6 °C, and the prefecture-specific daily mean temperature ranged from 9.4 °C in Hokkaido Prefecture to 17.4 °C in Fukuoka Prefecture (Figs. 1, S1 and Table S1 in the Supplement).

The variation in the mean temperature in the current period (2010–2019) and the projected increase at the end of the 21st century (2090–2099) in the four RCP scenarios in Japan are shown in Fig. 2 and Table 1. We projected a steep rise in mean temperatures under high-end emission scenarios (RCP6.0 and RCP8.5); however, this rise slowed or tended to be reduced after a number of decades under climate change scenarios that assume greenhouse gas mitigation policies (RCP2.6 and RCP4.5) (Figs. 2 and S2 in the Supplement). By the end of the 21st century, a drop in greenhouse gas emissions may avert warming in Japan, with a mean rise in temperature of 0.6 °C (range: 0.4–0.9) under RCP2.6 compared to 4.0 °C (range: 3.0–4.9) under RCP8.5. The respective data from each prefecture are shown in Figs. S2 and S3 in the Supplement.

Projected trends in heat- and cold-related excess morbidity according to three RCPs in Japan are summarized in Fig. 3 and Table 1. Our findings showed a common pattern of a reduction in cold-related morbidity

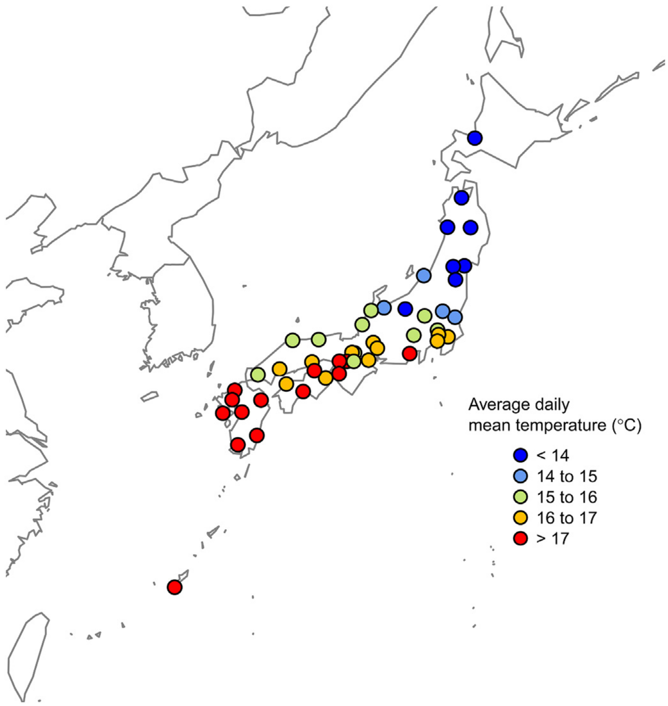


Fig. 1. The geographic distribution of the 47 Japanese prefectures and climate stations. The colors represent different ranges of mean daily temperature during the study period.

and mild rise in excess morbidity due to heat across the scenarios. The projected slopes were steeper under RCP8.5, while the trends were shallower throughout the 21st century under scenarios that assume mitigation strategies. Cold-related excess morbidity is projected to be reduced from 19.9% (95% eCI: −0.1, 33.4) in 2010–2019 to 13.8% (95% eCI: −2.5, 25.5) in 2090–2099 under scenarios of intense warming (RCP8.5), and there is a large degree of uncertainty for cold-related morbidity. In contrast, heat-related excess morbidity is projected to rise from 0.4% (95% eCI: 0.1, 0.6) to 2.4% (95% eCI: 0.5, 4.2) across the same period and conditions. The respective data from each prefecture are shown in Figs. S4 and S5 in the Supplement.

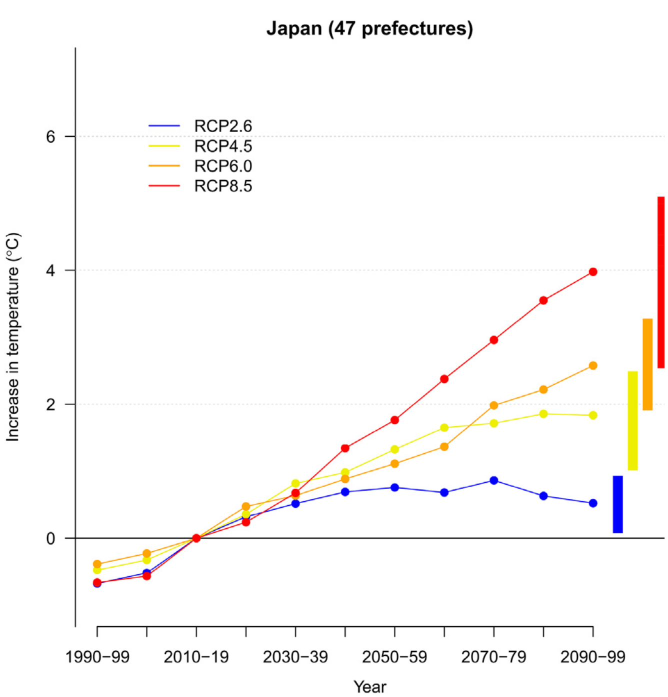


Fig. 2. Decadal temperature trends in Japan by scenario. The graph shows the projected increase in temperature (°C, GCM-ensemble average), averaged by decade and climate change scenario, compared to the current period (2010–2019). GCM = general circulation model.

Temporal changes in excess morbidity under three different RCPs in Japan are summarized in Fig. 4 and Table 1. There was a marked net reduction in excess morbidity, ranging from −0.8% (95% eCI −1.9, 0.1) under RCP2.6 to −4.2% (95% eCI −8.3, −0.1) under RCP8.5. The respective data from each prefecture are shown in Fig. S6 and Tables S2–S5 in the Supplement.

The sensitivity analysis revealed that varying the choice of model had little effect on the estimates (Table S6 in the Supplement).

4. Discussion

We investigated projections of the nationwide impact of temperature on OHCA in Japan according to different climate change scenarios using recently developed study designs and advanced statistical methods. We found that temperature-related excess morbidity is expected to be reduced under higher emission scenarios. To our knowledge, our study is the first to investigate the possible impact of temperature changes according to climate change scenarios on OHCA. Our findings indicate that climate change may have positive effects on OHCA.

Our study shows that climate change may possibly result in a marked reduction in temperature-related OHCA. We also found a steep reduction in cold-related excess morbidity under higher emission scenarios of global warming, and a small increase in heat-related excess morbidity. These findings agree with those of recent studies, which predict that lower intensity warming and bigger reductions in cold-related excess mortality could stimulate a minimal negative net effect in temperate areas, including Japan (Gasparrini et al., 2017). Moreover, temperature-related mortality due to acute ischemic heart disease is projected to remain stable over time under changing climate conditions in China (Li et al., 2018). However, another study in China projected that temperature-related cardiovascular disease mortality will increase under different RCP scenarios (Zhang et al., 2018). These findings indicate that ambient temperatures may impact the various subtypes of cardiovascular diseases in differing ways (Lin et al., 2009). Further, the mechanisms governing cardiac events involve multiple factors and complex interactions (Woodhouse et al., 1994). Although the physiological mechanism underlying temperature-related cardiovascular events remains to be elucidated, our results emphasize the need for additional studies on the projections of temperature-related excess morbidity for cardiovascular diseases.

The net reduction in OHCA as a result of global warming may be explained by several mechanisms. First, increasing temperature due to global warming may reduce health problems related to low temperatures, which can lead to offset the increase in morbidity by high temperatures. A recent study has shown that, although both high and low temperatures are responsible for OHCA burden, most OHCA cases are attributable to low temperatures (Onozuka and Hagihara, 2017c). Regarding low temperature-related health problems, recent studies have indicated that circulatory and coronary heart disease and ST-elevation myocardial infarction (STEMI) mortality is increased with low temperatures (Schwartz et al., 2015). It is possible that low temperatures trigger sympathetic stimulation and a rise in cardiac workload, which could stress a person with severe coronary stenosis and/or advanced heart failure beyond their compensation threshold (Izzo Jr. et al., 1990; Schwartz et al., 2015; Wolf et al., 2009). Second, low temperatures may contribute to the cardiovascular stress response by increasing blood viscosity, changing heart rate variability, and impacting inflammatory responses (Keatinge et al., 1986). Low temperature periods have been linked to high excess risk of heart failure, arrhythmia, and

Table 1
Heat-related, cold-related, and net excess morbidity (%) with 95% eCI by period and climate change scenario in Japan.

Scenario	Projected increase in temperature (2090–2099 vs 2010–2019)	Effect	Period 2010–2019	2050–2059	2090–2099
RCP2.6	0.6 (0.4, 0.9)	Heat	0.4 (0.1, 0.6)	0.7 (0.2, 1.4)	0.6 (0.2, 0.9)
		Cold	19.9 (−0.1, 33.2)	18.6 (−0.9, 31.9)	18.9 (−0.7, 32.3)
		Net	–	−1.0 (−2.3, −0.1)	−0.8 (−1.9, 0.1)
RCP4.5	1.8 (1.4, 2.2)	Heat	0.3 (0.1, 0.5)	0.8 (0.2, 1.4)	1.0 (0.2, 1.8)
		Cold	20.1 (0.2, 33.4)	17.6 (−1.4, 30.7)	16.8 (−1.8, 29.8)
		Net	–	−2.0 (−3.1, −0.8)	−2.6 (−4.4, −0.8)
RCP6.0	2.5 (1.7, 3.0)	Heat	0.3 (0.1, 0.5)	0.6 (0.2, 1.0)	1.4 (0.3, 2.8)
		Cold	20.3 (0.3, 33.8)	18.2 (−1.1, 31.3)	15.9 (−2.1, 28.5)
		Net	–	−1.9 (−3.1, −0.9)	−3.4 (−5.7, −1.0)
RCP8.5	4.0 (3.0, 4.9)	Heat	0.4 (0.1, 0.6)	1.0 (0.3, 1.8)	2.4 (0.5, 4.2)
		Cold	19.9 (−0.1, 33.4)	16.8 (−1.8, 29.5)	13.8 (−2.5, 25.5)
		Net	–	−2.5 (−4.8, −0.5)	−4.2 (−8.3, −0.1)

Data on projected increase in temperature are average mean prefecture-specific temperature (range) as GCM-ensemble. RCP = representative concentration pathway. GCM = general circulation model.

atrial fibrillation (Medina-Ramon et al., 2006). Low temperatures raise sympathetic tone, blood pressure, vascular resistance, fibrinogen level, platelet count, some clotting factors, and blood viscosity, which can raise the risk of plaque rupture, thrombosis, and STEMI mortality (Izzo Jr. et al., 1990; Schwartz et al., 2015; Wolf et al., 2009). Furthermore, those with reduced vitamin D levels are vulnerable to sudden cardiac death during winter, suggesting that increasing vitamin D levels by adequate sun exposure in the winter months may be significant for decreasing sudden cardiac death (Deo et al., 2011; Drechsler et al., 2010; Giovannucci et al., 2008; Onozuka and Hagihara, 2017b, d). Our findings are therefore physiologically plausible and suggest that climate change according to different levels of future global warming may markedly reduce OHCA.

Our findings suggest that variations in temperature-related excess OHCA are proportional to the degree of global warming under each of the RCP emission scenarios. We found that the largest net reduction in excess morbidity was projected under RCP8.5, which assumes very high greenhouse gas emissions (Pachauri et al., 2014). In contrast, the net reduction in excess morbidity is lower under RCP2.6, which assumes a limited increase in global mean temperatures of 2 °C following climate change adaptation and mitigation policies (van Vuuren et al., 2011b). Although recent studies have reported the negative impacts of climate change on mortality (Gasparrini et al., 2017), there may be inconsistencies in the direction and magnitude of the impacts on mortality and morbidity due to climate change. Our results emphasize the importance of further investigation into projections of global warming and the associated impacts on mortality and morbidity due to different causes.

Our results have practical implications for refining or adjusting estimates for climate change-related OHCA in future public health policies. Our study projects a largest decrease in net excess OHCA morbidity due to climate change under high-emission scenarios. The majority of the excess morbidity was attributable to low temperatures, while heat was only associated with a small fraction of excess morbidity. Additionally, the reduction in temperature-related net excess morbidity is

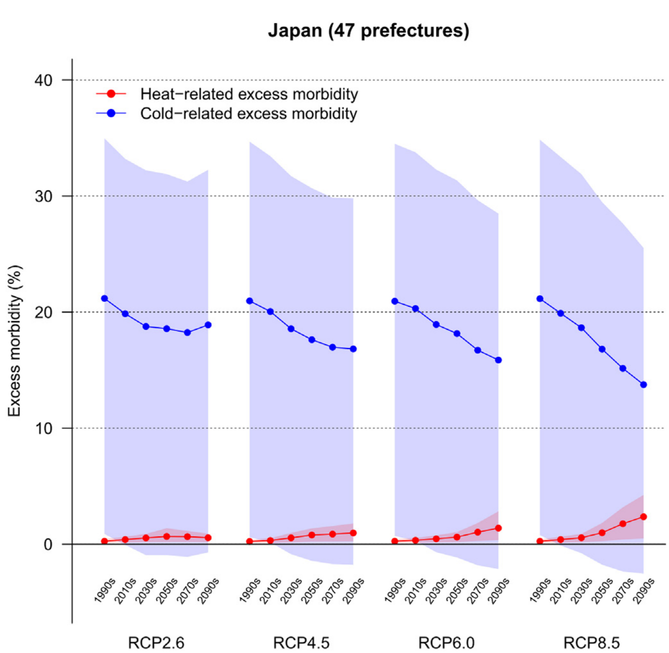


Fig. 3. Trends in heat-related and cold-related excess morbidity in Japan. The graph shows the excess morbidity by decade attributed to heat and cold under three climate change scenarios (RCP2.6, RCP4.5, RCP6.0, and RCP8.5). Estimates are reported as GCM-ensemble mean decadal fractions. The shaded areas represent 95% empirical confidence intervals (eCIs). RCP = representative concentration pathway; GCM = general circulation model.

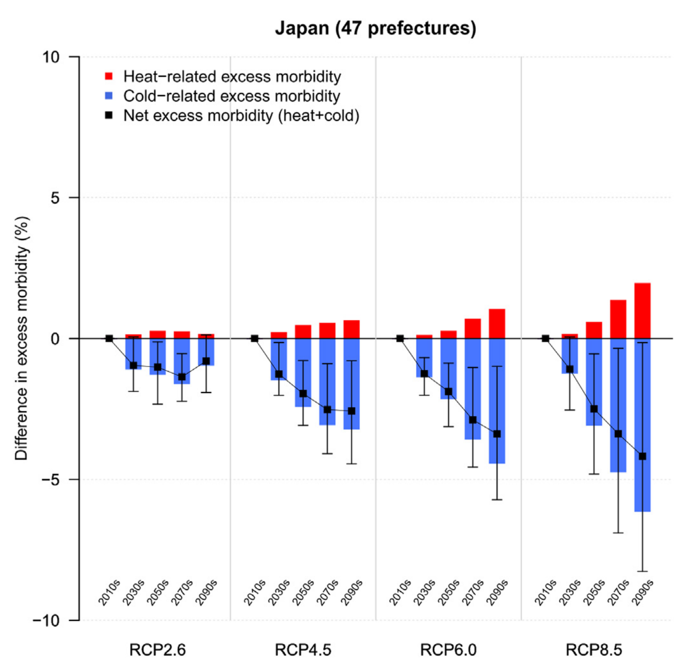


Fig. 4. Temporal change in excess morbidity in Japan. The graph shows the difference in excess morbidity by decade compared with 2010–2019 under three climate change scenarios (RCP2.6, RCP4.5, RCP6.0, and RCP8.5). Estimates are reported as GCM-ensemble means. The black vertical segments represent 95% empirical CIs (eCIs) of net difference. RCP = representative concentration pathway; GCM = general circulation model.

expected to be significant in scenarios of high greenhouse gas emissions. These findings are important for the development of disease-specific public health policies, and for informing the ongoing international discussion on the health impacts of climate change.

There were several limitations in our study. First, while our projections of temperature-OHCA relationships according to future warming scenarios enabled isolation of the effects of climate change, they did not account for important factors such as demographic changes and adaptation (Arbuthnott et al., 2016; Hajat et al., 2014; Nordio et al., 2015; O'Neill et al., 2014). Especially, since a recent study suggested that gender and age are vulnerability factors for the effect of temperature on OHCA (Onozuka and Hagihara, 2017c), demographic and adaptation changes in the future can alter the impact of climate change on OHCA. Therefore, our results should not be interpreted as predictions of future excess morbidity but rather possible outcomes under well-defined but hypothetical scenarios. Second, our projections of temperature-related excess morbidity are subject to considerable uncertainty, especially those associated with the net impact, because of both variability in the climate models and imprecision in the predicted exposure-response correlation (Benmarhnia et al., 2014). Third, we used available outdoor monitoring data from one representative weather station to represent population exposure to the mean temperature. Thus, exposure measurement bias and misclassification should not be ignored. These factors might affect the interpretation of our findings, and additional studies using more precise modeling methods are required to resolve these issues.

In summary, our study indicates that Japan is projected to experience a substantial net reduction in OHCA under higher-emission scenarios. The decrease in risk is limited to a specific morbidity cause, and a broader assessment of cardiovascular disease morbidity within climate change scenarios should consider other direct and indirect impacts.

Acknowledgments

We thank Manabu Hasegawa, Takuya Ishizaka, and Kenji Nakanishi for their assistance with acquiring data from the Fire and Disaster Management Agency of the Ministry of Internal Affairs and Communications, Japan.

Financial disclosure

This work was supported by the Japan Society for the Promotion of Science (JSPS) KAKENHI Grant Numbers 15K08714, 16H05247, 18K11666, and 19H03900; the Medical Research Council UK (Grant ID: MR/M022625/1); and the Natural Environment Research Council UK (Grant ID: NE/R009384/1). The funding sources had no role in the study design, data collection, data analysis, data interpretation, or preparation of the manuscript.

Author contributions

DO made substantial contributions to conception and design, did the statistical analysis, took the lead in drafting the manuscript, and interpreting the results. DO, AG, and FS developed the statistical methods. MH and YH provided data and substantial scientific input in interpreting the results and drafting the manuscript. All gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

Declaration of competing interest

The authors declare that they have no competing interests.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2019.05.196.

References

Arbuthnott, K., Hajat, S., Heaviside, C., Vardoulakis, S., 2016. Changes in population susceptibility to heat and cold over time: assessing adaptation to climate change. Environ. Health 15 (Suppl. 1), 33.

Benmarhnia, T., Sottile, M.F., Plante, C., Brand, A., Casati, B., Fournier, M., et al., 2014. Variability in temperature-related mortality projections under climate change. Environ. Health Perspect. 122, 1293–1298.

Bentsen, M., Bethke, I., Debernard, J.B., Iversen, T., Kirkevåg, A., Seland, Ø., et al., 2013. The Norwegian Earth System Model, NorESM1-M–part 1: description and basic evaluation of the physical climate. Geosci. Model Dev. 6, 687–720.

Deo, R., Katz, R., Shlipak, M.G., Sotoodehnia, N., Psaty, B.M., Sarnak, M.J., et al., 2011. Vitamin D, parathyroid hormone, and sudden cardiac death: results from the Cardiovascular Health Study. Hypertension 58, 1021–1028.

Drechsler, C., Pilz, S., Obermayer-Pietsch, B., Verduijn, M., Tomaschitz, A., Krane, V., et al., 2010. Vitamin D deficiency is associated with sudden cardiac death, combined cardiovascular events, and mortality in haemodialysis patients. Eur. Heart J. 31, 2253–2261.

Dunne, J.P., John, J.G., Adcroft, A.J., Griffies, S.M., Hallberg, R.W., Shevliakova, E., et al., 2012. GFDL's ESM2 global coupled climate–carbon earth system models. Part I: physical formulation and baseline simulation characteristics. J. Clim. 25, 6646–6665.

Dunne, J.P., John, J.G., Shevliakova, E., Stouffer, R.J., Krasting, J.P., Malyshev, S.L., et al., 2013. GFDL's ESM2 global coupled climate–carbon earth system models. Part II: carbon system formulation and baseline simulation characteristics. J. Clim. 26, 2247–2267.

Field, J.M., Hazinski, M.F., Sayre, M.R., Chameides, L., Schexnayder, S.M., Hemphill, R., et al., 2010. Part 1: executive summary: 2010 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation 122, S640–S656.

Gasparrini, A., Guo, Y., Hashizume, M., Lavigne, E., Tobias, A., Zanobetti, A., et al., 2016. Changes in Susceptibility to Heat During the Summer: A Multicountry Analysis. Am. J. Epidemiol. 183, 1027–1036.

Gasparrini, A., Guo, Y., Sera, F., Vicedo-Cabrera, A.M., Huber, V., Tong, S., et al., 2017. Projections of temperature-related excess mortality under climate change scenarios. Lancet Planet Health 1, e360–e367.

Giovannucci, E., Liu, Y., Hollis, B.W., Rimm, E.B., 2008. 25-hydroxyvitamin D and risk of myocardial infarction in men: a prospective study. Arch. Intern. Med. 168, 1174–1180.

Guo, Y., Barnett, A.G., Pan, X., Yu, W., Tong, S., 2011. The impact of temperature on mortality in Tianjin, China: a case-crossover design with a distributed lag nonlinear model. Environ. Health Perspect. 119, 1719–1725.

Guo, Y., Gasparrini, A., Armstrong, B., Li, S., Tawatsupa, B., Tobias, A., et al., 2014. Global variation in the effects of ambient temperature on mortality: a systematic evaluation. Epidemiology 25, 781–789.

Hagihara, A., Hasegawa, M., Abe, T., Nagata, T., Wakata, Y., Miyazaki, S., 2012. Prehospital epinephrine use and survival among patients with out-of-hospital cardiac arrest. JAMA 307, 1161–1168.

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, 641–648.

Hempel, S., Frieler, K., Warszawski, L., Schewe, J., Piontek, F., 2013. A trend-preserving bias correction – the ISI-MIP approach. Earth Syst. Dynam. 4, 219–236.

Iversen, T., Bentsen, M., Bethke, I., Debernard, J.B., Kirkevåg, A., Seland, Ø., et al., 2013. The Norwegian Earth System Model, NorESM1-M–part 2: climate response and scenario projections. Geosci. Model Dev. 6, 389–415.

Izzo Jr., J.L., Larrabee, P.S., Sander, E., Lillis, L.M., 1990. Hemodynamics of seasonal adaptation. Am. J. Hypertens. 3, 405–407.

Jones, C.D., Hughes, J.K., Bellouin, N., Hardiman, S.C., Jones, G.S., Knight, J., et al., 2011. The HadGEM2-ES implementation of CMIP5 centennial simulations. Geosci. Model Dev. 4, 543–570.

Keatinge, W.R., Coleshaw, S.R., Easton, J.C., Cotter, F., Mattock, M.B., Chelliah, R., 1986. Increased platelet and red cell counts, blood viscosity, and plasma cholesterol levels during heat stress, and mortality from coronary and cerebral thrombosis. Am. J. Med. 81, 795–800.

Kitamura, T., Kiyohara, K., Sakai, T., Matsuyama, T., Hatakeyama, T., Shimamoto, T., et al., 2016. Public-access defibrillation and out-of-hospital cardiac arrest in Japan. N. Engl. J. Med. 375, 1649–1659.

Lee, J.Y., Kim, H., 2016. Projection of future temperature-related mortality due to climate and demographic changes. Environ. Int. 94, 489–494.

Li, T., Horton, R.M., Bader, D.A., Liu, F., Sun, Q., Kinney, P.L., 2018. Long-term projections of temperature-related mortality risks for ischemic stroke, hemorrhagic stroke, and acute ischemic heart disease under changing climate in Beijing, China. Environ. Int. 112, 1–9.

Lin, S., Luo, M., Walker, R.J., Liu, X., Hwang, S.A., Chinery, R., 2009. Extreme high temperatures and hospital admissions for respiratory and cardiovascular diseases. Epidemiology 20, 738–746.

Medina-Ramon, M., Zanobetti, A., Cavanagh, D.P., Schwartz, J., 2006. Extreme temperatures and mortality: assessing effect modification by personal characteristics and specific cause of death in a multi-city case-only analysis. Environ. Health Perspect. 114, 1331–1336.

Mignot, J., Bony, S., 2013. Presentation and analysis of the IPSL and CNRM climate models used in CMIP5. Clim. Dyn. 40, 2089.

Mozaffarian, D., Benjamin, E.J., Go, A.S., Arnett, D.K., Blaha, M.J., Cushman, M., et al., 2015. Heart disease and stroke statistics—2015 update: a report from the American Heart Association. Circulation 131, e29–322.

Nichol, G., Thomas, E., Callaway, C.W., Hedges, J., Powell, J.L., Aufderheide, T.P., et al., 2008. Regional variation in out-of-hospital cardiac arrest incidence and outcome. JAMA 300, 1423–1431.

Nordio, F., Zanobetti, A., Colicino, E., Kloog, I., Schwartz, J., 2015. Changing patterns of the temperature-mortality association by time and location in the US, and implications for climate change. Environ. Int. 81, 80–86.

O'Neill, B.C., Kriegler, E., Riahi, K., Ebi, K.L., Hallegatte, S., Carter, T.R., et al., 2014. A new scenario framework for climate change research: the concept of shared socioeconomic pathways. Clim. Chang. 122, 387–400.

Onozuka, D., Hagihara, A., 2017a. Extreme temperature and out-of-hospital cardiac arrest in Japan: a nationwide, retrospective, observational study. Sci. Total Environ. 575, 258–264.

Onozuka, D., Hagihara, A., 2017b. Out-of-hospital cardiac arrest attributable to sunshine: a nationwide, retrospective, observational study. Eur. Heart J. Qual. Care Clin. Outcomes 3, 107–113.

Onozuka, D., Hagihara, A., 2017c. Out-of-hospital cardiac arrest risk attributable to temperature in Japan. Sci. Rep. 7, 39538.

Onozuka, D., Hagihara, A., 2017d. Solar radiation and out-of-hospital cardiac arrest in Japan. Environ. Pollut. 230, 46–52.

Onozuka, D., Hagihara, A., 2017e. Spatiotemporal variation in heat-related out-of-hospital cardiac arrest during the summer in Japan. Sci. Total Environ. 583, 401–407.

Pachauri, R.K., Allen, M.R., Barros, V.R., Broome, J., Cramer, W., Christ, R., et al., 2014. Climate change 2014: synthesis report. Contribution of Working Groups I, II and III to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change. IPCC.

Patz, J.A., Campbell-Lendrum, D., Holloway, T., Foley, J.A., 2005. Impact of regional climate change on human health. Nature 438, 310–317.

Schwartz, B.G., Qualls, C., Kloner, R.A., Laskey, W.K., 2015. Relation of total and cardiovascular death rates to climate system, temperature, barometric pressure, and respiratory infection. Am. J. Cardiol. 116, 1290–1297.

Taylor, K.E., Stouffer, R.J., Meehl, G.A., 2012. An overview of CMIP5 and the experiment design. Bull. Am. Meteorol. Soc. 93, 485–498.

Tian, L., Qiu, H., 2017. Environmental factors and out-of-hospital cardiac arrest. Eur. Heart J. Qual. Care Clin. Outcomes 3, 97–98.

van Vuuren, D.P., Edmonds, J., Kainuma, M., Riahi, K., Thomson, A., Hibbard, K., et al., 2011a. The representative concentration pathways: an overview. Clim. Chang. 109, 5.

van Vuuren, D.P., Stehfest, E., den Elzen, M.G.J., Kram, T., van Vliet, J., Deetman, S., et al., 2011b. RCP2.6: exploring the possibility to keep global mean temperature increase below 2°C. Clim. Chang. 109, 95.

Vicedo-Cabrera, A.M., Sera, F., Gasparrini, A., 2019. Hands-on tutorial on a modeling framework for projections of climate change impacts on health. Epidemiology 30, 321–329.

Warszawski, L., Frieler, K., Huber, V., Piontek, F., Serdeczny, O., Schewe, J., 2014. The Inter-Sectoral Impact Model Intercomparison Project (ISI-MIP): project framework. Proc. Natl. Acad. Sci. U. S. A. 111, 3228–3232.

Watanabe, S., Hajima, T., Sudo, K., Nagashima, T., Takemura, T., Okajima, H., et al., 2011. MIROC-ESM 2010: model description and basic results of CMIP5-20c3m experiments. Geosci. Model Dev. 4, 845–872.

Watts, N., Adger, W.N., Agnolucci, P., Blackstock, J., Byass, P., Cai, W., et al., 2015. Health and climate change: policy responses to protect public health. Lancet 386, 1861–1914.

Wissenberg, M., Lippert, F.K., Folke, F., Weeke, P., Hansen, C.M., Christensen, E.F., et al., 2013. Association of national initiatives to improve cardiac arrest management with rates of bystander intervention and patient survival after out-of-hospital cardiac arrest. JAMA 310, 1377–1384.

Wolf, K., Schneider, A., Breitner, S., von Klot, S., Meisinger, C., Cyrys, J., et al., 2009. Air temperature and the occurrence of myocardial infarction in Augsburg, Germany. Circulation 120, 735–742.

Woodhouse, P.R., Khaw, K.T., Plummer, M., Foley, A., Meade, T.W., 1994. Seasonal variations of plasma fibrinogen and factor VII activity in the elderly: winter infections and death from cardiovascular disease. Lancet 343, 435–439.

Zhang, Y., Yu, C., Bao, J., Li, X., 2017. Impact of temperature on mortality in Hubei, China: a multi-county time series analysis. Sci. Rep. 7, 45093.

Zhang, B., Li, G., Ma, Y., Pan, X., 2018. Projection of temperature-related mortality due to cardiovascular disease in Beijing under different climate change, population, and adaptation scenarios. Environ. Res. 162, 152–159.

Zhang, Y., Xiang, Q., Yu, Y., Zhan, Z., Hu, K., Ding, Z., 2019. Socio-geographic disparity in cardiorespiratory mortality burden attributable to ambient temperature in the United States. Environ. Sci. Pollut. Res. Int. 26, 694–705.