

Non-optimal temperature-attributable mortality and morbidity burden by cause, age and sex under climate and population change scenarios: a nationwide modelling study in Japan

Lei Yuan,^a Lina Madaniyazi,^b Ana M. Vicedo-Cabrera,^{c,d} Chris Fook Sheng Ng,^a Kazutaka Oka,^e Paul L. C. Chua,^a Kayo Ueda,^f Aurelio Tobias,^{b,g} Yasushi Honda,^{b,e} and Masahiro Hashizume^{a,b,*}

^aDepartment of Global Health Policy, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

^bSchool of Tropical Medicine and Global Health, Nagasaki University, Nagasaki, Japan

^cInstitute of Social and Preventive Medicine (ISPM), University of Bern, Bern, Switzerland

^dOeschger Center for Climate Change Research (OCCR), University of Bern, Bern, Switzerland

^eCenter for Climate Change Adaptation, National Institute for Environmental Studies, Tsukuba, Ibaraki, Japan

^fDepartment of Hygiene, Graduate School of Medicine, Hokkaido University, Sapporo, Hokkaido, Japan

^gInstitute of Environmental Assessment and Water Research (IDAEA), Spanish Council for Scientific Research (CSIC), Barcelona, Spain

Summary

Background Future temperature effects on mortality and morbidity may differ. However, studies comparing projected future temperature-attributable mortality and morbidity in the same setting are limited. Moreover, these studies did not consider future population change, human adaptation, and the variations in subpopulation susceptibility. Thus, we simultaneously projected the temperature-related mortality and morbidity by cause, age, and sex under population change, and human adaptation scenarios in Japan, a super-ageing society.

Methods We used daily mean temperatures, mortality, and emergency ambulance dispatch (a sensitive indicator for morbidity) in 47 prefectures of Japan from 2015 to 2019 as the reference for future projections. Future mortality and morbidity were generated at prefecture level using four shared socioeconomic pathway (SSP) scenarios considering population changes. We calculated future temperature-related mortality and morbidity by combining baseline values with future temperatures and existing temperature risk functions by cause (all-cause, circulatory, respiratory), age (<65 years, ≥65 years), and sex under various climate change and SSP scenarios (SSP1-2.6, SSP2-4.5, SSP3-7.0, and SSP5-8.5). Full human adaptation was simulated based on empirical evidence using a fixed percentile of minimum mortality or morbidity temperature (MMT), while no adaptation was simulated with a fixed absolute MMT.

Findings A future temporal decline in mortality burden attributable to non-optimal temperatures was observed, driven by greater cold-related deaths than heat-related deaths. In contrast, temperature-related morbidity increased over time, which was primarily driven by heat. In the 2050s and 2090s, under a moderate scenario, there are 83.69 (95% empirical confidence interval [eCI] 38.32–124.97) and 77.31 (95% eCI 36.84–114.47) all-cause deaths per 100,000 population, while there are 345.07 (95% eCI 258.31–438.66) and 379.62 (95% eCI 271.45–509.05) all-cause morbidity associated with non-optimal temperatures. These trends were largely consistent across causes, age, and sex groups. Future heat-attributable health burden is projected to increase substantially, with spatiotemporal variations and is particularly pronounced among individuals ≥65 y and males. Full human adaptation could yield a decreasing temperature-attributable mortality and morbidity in line with a decreasing population.

Interpretation Our findings could support the development of targeted mitigation and adaptation strategies to address future heat-related impacts effectively. This includes improved healthcare allocations for ambulance dispatch and hospital preventive measures during heat periods, particularly custom-tailored to address specific health outcomes and vulnerable subpopulations.

Funding Japan Science and Technology Agency and Environmental Restoration and Conservation Agency and Ministry of the Environment of Japan.

*Corresponding author. Department of Global Health Policy, Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo, 113-0033, Japan.

E-mail address: hashizume@m.u-tokyo.ac.jp (M. Hashizume).



The Lancet Regional Health - Western Pacific 2024;52: 101214

Published Online xxx
<https://doi.org/10.1016/j.lanwpc.2024.101214>

Copyright © 2024 The Author(s). Published by Elsevier Ltd. This is an open access article under the CC BY-NC license (<http://creativecommons.org/licenses/by-nc/4.0/>).

Keywords: Climate change; Non-optimal temperature; Mortality; Morbidity; Population ageing; Attributable risk

Research in context

Evidence before this study

Extensive modeling evidence indicates the relationship between projected temperature changes and expected increase in heat-related mortality and morbidity in the future. While the link between temperature and climate-sensitive health outcomes appears straightforward, it is, in fact, far more complicated due to the different mechanisms through which climate can exert fatal and non-fatal health impacts, and such discrepancy in temperature effects on both health endpoints can be influenced by cause of diseases, age, and sex. We searched PubMed, Web of Science, and Google Scholar for articles published in English that project the temperature-related mortality and morbidity to explore extent of available evidence on 30th October 2023. We used a combination of search terms, including terms “temperature”, and “heat” for exposure, and “mortality”, “death”, “excess death”, “morbidity”, “hospitalization”, “emergency room visit”, “inpatient visit”, “outpatient visit”, “emergency ambulance”, and “excess morbidity” for outcomes, and the terms “project”, “future”. Three studies estimated future effects of temperature on both mortality and morbidity within the same study setting. They revealed the possible differences in the future burden of temperature-related mortality and morbidity, but in the absence of population change, future adaptation or the impacts on vulnerable subpopulations.

Added value of this study

To the best of our knowledge, this study is the first to provide a comprehensive overview of future mortality and morbidity burden attributable to non-optimal temperatures by cause of disease, age, and sex. Contrasting patterns of non-optimal temperature-related mortality and morbidity are found. The projected non-optimal temperature-attributable mortality is driven by greater cold-related mortality than heat-related mortality, resulting in a net reduction. By contrast, the morbidity is projected to substantially rise, dominated by larger heat-related morbidity. These changes in temperature-related health burdens vary across subpopulations by age and sex, also across prefectures, with population aged 65 years and older, males, and those living in prefectures with larger temperature increase or severe population decline are expected to sustain a higher rise in burden. Furthermore, future cold- and heat-related mortality and morbidity burden would be greatly reduced under population adaptation scenarios.

Implications of all the available evidence

This research has important implications for policymakers to protect the most vulnerable populations and identify local strategies to design targeted mitigation and adaptation policies. It also highlights the need to tackle the possible future additional heat-related morbidity requiring substantial medical resources and possible expansion of secondary healthcare infrastructure.

Introduction

Numerous studies have been conducted to project the impact of non-optimal temperatures on health under climate change, with the associated mortality and morbidity expected to increase with a warmer climate.^{1–4} However, obtaining more precise estimates of future excess health burden remains a challenge due to substantial variations in susceptibility to non-optimal temperatures across fatal and non-fatal health endpoints. Distinct patterns have been observed for the association of temperature with mortality and morbidity, indicating different mechanisms by which temperature triggers these endpoints.^{5–7} These disparities could be attributed to variations in susceptible subpopulations by specific causes, sex, and age groups.^{8,9} Moreover, subnational differences in climatic, socioeconomic and demographic conditions contribute to geographical disparities in susceptibility to temperature-related risks.^{10,11} To date, few projection studies have estimated the impact of future temperature on both mortality and morbidity

simultaneously within a unified framework at local or country level.^{2,4,12} Additionally, little is known about future heat- and cold-attributable mortality and morbidity among population subgroups, particularly the most susceptible population by cause, age, sex and subnational level.^{13,14} These absences of consideration for susceptible populations limit the interpretability of the projection results and the design of effective climate interventions.

Another limitation of many existing projection studies is the assumption of a constant population in the future.^{2,15–20} Estimation of the future temperature-related health impacts could be less realistic without considering future population changes, in terms of population size and ageing.^{21,22} In Japan, future population size is projected to decrease over time, concurrent with a sustained increase in the proportion of older population.^{23–25} It is reasonable to suspect that such intensified population ageing, along with rising temperatures would exacerbate heat-related health burden for older adults, as they are particularly vulnerable to risks from non-

optimal temperatures.^{26,27} No study before has provided explicit estimates of future mortality from non-optimal temperature while accounting for demographic changes in Japanese population.

Enhanced understanding of future temperature impact combined with population scenarios is crucial not only for Japan, a super-ageing nation at the forefront of global ageing, but also for other advanced countries expected to experience similar demographic shifts. This insight could serve as a valuable asset when envisioning the future of other developed nations, aiding in the development of effective public health and climate adaptation strategies to safeguard the most vulnerable populations.²⁸

In this study, we projected nationwide and sub-national future temperature-attributable mortality and morbidity in Japan from 2010 to 2099, considering multiple scenarios of climate change and population dynamics. Our examination emphasized variations in susceptibility across causes, age and sex. The evidence presented in this temperature-attributable impact projection is specifically tailored to disease outcomes and vulnerable populations and is critical for the development of targeted mitigation and adaptation policies.

Methods

Data sources and scenario models

We used the temperature risk curves for morbidity and mortality from our recent study in Japan.⁹ The risk curves we used were for the period 2015–2019 and were available by cause (all-cause, circulatory, respiratory), age group (<65 years of age; ≥65 years of age), and sex for each of the 47 prefectures. These temperature risk curves were modelled using historical data of observed temperatures from the Japan Meteorological Agency, recorded deaths from the Ministry of Health, Labor and Welfare of Japan, and morbidity cases identified through emergency ambulance dispatch (EAD) data provided by the Fire and Disaster Management Agency of the Ministry of Internal Affairs and Communications. Ethical approval was not required since all data collected in this study was secondary data without any personal information and not transferable.

We obtained the projected daily temperatures from the Inter-Sectoral Impact Model Intercomparison Project (ISIMIP) 3b simulation round based on several general circulation models (GCMs) from phase 6 of the Coupled Model Intercomparison Project (CMIP6) outputs.^{29,30} The ISIMIP3b database provides daily near-surface air temperature for historical climate simulations (1850–2014) and future simulation periods (2015–2099) periods, bias-corrected up to 2019, and downscaled at a $0.5^\circ \times 0.5^\circ$ spatial resolution. The projected temperatures are available in 5 future scenarios: SSP1-2.6, SSP2-4.5, SSP3-7.0, SSP4-6.0 and SSP5-8.5. The future scenario is the combination of five shared socio-economic pathways (SSPs; specifically SSP1

depicting sustainable development, SSP2 depicting intermediate challenges, SSP3 depicting regional conflict, SSP4 depicting unequal development, and SSP5 depicting fossil fuel dependence), and four representative concentration pathways (RCPs) representing with radiative forcing of 2.6, 4.5, 6.0, and 8.5 W/m^2 .^{14,31,32} In each scenario (SSP1, SSP2, SSP3), challenges encompass three levels (low, medium, high) for both mitigation and adaptation strategies, while under SSP5, mitigation challenges remain low, but adaptation challenges are notably high.³¹ We selected projected temperatures from four future scenarios (SSP1-2.6, SSP2-4.5, SSP3-7.0, and SSP5-8.5) based on five GCMs (GFDL-ESM4, IPSL-CM6A-LR, MPI-ESM1-2 h, MRI-ESM2-0, and UKESM1-0-LL) because the other future scenarios were only available on a few GCMs (Supplementary text). We then extracted the average temperatures in each SSP-based scenario and for each prefecture in Japan during 1972–2099. The modelled temperature time series were recalibrated using observed temperatures available from the weather station data for each prefecture (1972–2019) to avoid deviations between observed and simulated historical temperature distributions while preserving predicted temperature trends (Figure S1).³³

Projection of future mortality and morbidity time-series

Projected Japanese population data under specific SSP scenarios (SSP_i) was collected from the National Institute for Environmental Studies (NIES). SSP_i-specific population projections are narratives of future demographic and societal developments in Japan indicating variable combinations of fertility, mortality, mobility, and non-permanent residents.^{34,35} The population projections at the prefecture level for each 5-year blocks from 2015 to 2100 were obtained from SSP_i. These projections are based on various prefecture-level factors, including the child-female ratio, sex ratio of 0–4-year-old, survival rate, and migration rate for each sex and age group in the base year in each prefecture. For future periods, the projected population for each 5-year age group is determined by multiplying the projected population by the assumed parameter values. Here, the assumptions of future population growth used for each scenario are high fertility, medium mortality and immigration rates under SSP1, medium growth in fertility, mortality and immigration for SSP2, low fertility, medium mortality and immigration rates for SSP3, and a high growth scenario under SSP5, assuming medium fertility and mortality rates, with high immigration (Table S1).³⁴

We linearly interpolated data for different sex and age groups by 5-year blocks into annual values from 2010 to 2100 in each prefecture. The annual average of daily mortality or morbidity rate by cause, age and sex was computed as the average for each day of the year in the prefecture during 2015–2019, divided by the respective annual average population. The daily

mortality or morbidity rates for 365 days were then multiplied with the respective annual population projection for 2010–2100 to obtain the final prefecture-level historical and projected series of daily mortality or morbidity counts for different cause, age, and sex groups.¹²

Projection of temperature-attributable mortality and morbidity burden

We generated prefecture-specific risk functions for temperature-mortality and temperature-morbidity associations using a two-stage analysis, extending a method previously applied (see Supplementary detailed information on the statistical analysis).⁹ In brief, we replaced the previously used quadratic B-spline for the exposure–response modelling with a natural cubic B-spline in the first stage, which allows a log-linear extrapolation of the functions beyond the boundaries of observed temperature range.^{36,37} In the second stage, we performed a multivariate meta-regression to pool the reduced estimates of the overall cumulative exposure–response curves and to derive the best linear unbiased prediction of the coefficients in each prefecture.^{38,39} The temperature corresponding to the minimum mortality or morbidity risk is chosen as a reference and interpreted as the prefecture-specific optimal temperature (MMT).⁴⁰

For each day in each prefecture, we applied the above-mentioned prefecture-specific temperature risk curve to daily temperature to calculate the daily attributable fraction (AF) and attributable numbers (ANs) for mortality and morbidity over the lag period.⁴¹ The total excess mortality or morbidity associated with non-optimal temperatures is the sum of the contributions of all days in the time series. To distinguish the effects of cold and hot, we separate these components by summing over the subset of days with temperatures below or above MMT, respectively.³⁶ The ratio of the ANs to the total mortality or morbidity counts is the total AF. We calculated separately the excess mortality and morbidity for each prefecture and under each combination of GCMs and SSPs. We then computed AFs as GCM-ensemble averages by aggregating by prefecture and country, decade, and SSP, using the corresponding total number of mortality or morbidity as the denominator. Uncertainties in both estimates of risk functions and variability in temperature projections across GCMs and SSPs were quantified by generating 1000 samples of coefficients through Monte Carlo simulations assuming a Gaussian multivariate distribution.^{12,36} Uncertainties are reported as 95% empirical confidence intervals (95% eCIs), derived from the 2.5th and 97.5th percentiles of the 1000 sample distributions.⁴² The temperature-attributable mortality or morbidity rate for each population was further derived by dividing ANs of the mortality or morbidity by the relevant population size, defined in this study as the burden attributable to temperature.⁴³ The fold change between the temperature-

attributable mortality and morbidity from the end of this century and the baseline period is calculated to quantify the relative differences, indicating how much future burden has changed from baseline. Estimates were done by cause, age and sex groups.

Adaptation analysis

We also explored possible human adaptation scenario for threshold (MMT) by applying a constant relative threshold for each prefecture that aligns with its progressively higher mean temperature. This self-empirical scenario was initially proposed based on a 37-year nationwide observations of heat-related all-cause mortality in Japan, assuming a fixed MMT percentile (MMTP) obtained from the observational exposure–response relationships in the future to be “full adaptation”.⁴⁴ Moreover, another local study examining empirical relationship between mean temperature and mortality in nationwide Japan over the past 41 years also indicated an increasing higher MMTP by cause, age and sex.¹⁰ Therefore, the adopted assumption of a constant MMTP to model future adaptation in this research is deemed modest and more realistic.⁴⁵

Software

All analyses were performed with R (version 4.2.1), using *dlnm*, and *mixmeta* packages. The R code for the analysis is available on request. We provide details of the applied adaptation analysis at the personal web page of the first author (<https://github.com/YuanILei>).

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication after obtaining approval from all coauthors.

Results

Between 2015 and 2019, a daily mean of 77.8, 20.2, and 11.5 deaths due to all-cause, circulatory, and respiratory causes were observed at prefecture level, respectively (Table S2).⁹ The daily mean count of all-cause, circulatory, and respiratory EAD was 300.4, 26.2, and 15.5. Both average mean mortality and morbidity show the wide ranges across prefectures. More than 90% of mortality and 60% of morbidity cases were from people aged 65 years and older, respectively. The average daily mean temperature of the 47 prefectures was 16.0 °C, ranging from 9.6 to 23.8 °C.

The projected increase in daily mean temperature by 2090–2099 compared to 2010–2019 is expected to be smallest (0.95 °C) under the sustainability pathway SSP1-2.6, and the greatest increase of 4.70 °C under the high-end emission scenario SSP5-8.5 (Fig. 1A,

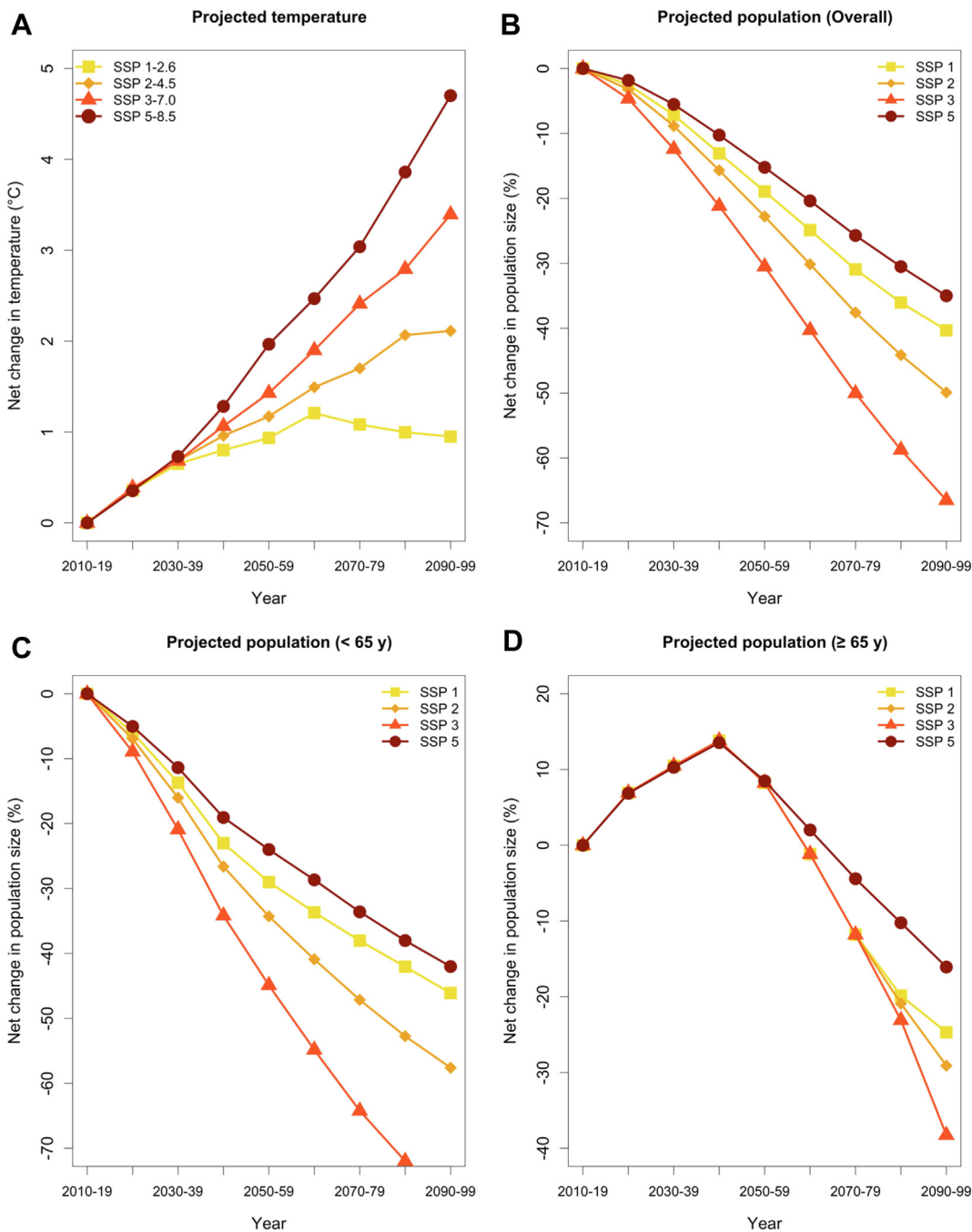


Fig. 1: Temporal trends in projected temperature increase by climate change scenarios and projected population change by shared socio-economic pathway (SSP), relative to baseline period (2010–19) in Japan. Please note that the scale of each figure is distinct. Corresponding numeric data are presented in Tables S3 and S5.

Table S3). Unlike the sustained steep temperature increases in the coming decades under the high-end emissions scenarios (SSP3-7.0 and SSP5-8.5), SSP1-2.6 and SSP2-4.5 have gradual temporal increases assuming mitigation policies to limit greenhouse gas emissions

(Fig. 1A). Future temperature increases for prefectures showed some geographical differences, with a smaller increase in temperature for prefectures located in the southern region than northern prefectures. For example, 3.3 °C for the southernmost Okinawa

prefecture and up to 5.5 °C in the northernmost Hokkaido prefecture under SSP5-8.5 by 2090–2099 (Table S4, Figure S2).

The projected Japanese population generally declined with varied magnitudes under different SSPs, with the lowest decline under SSP5 and the highest decline under SSP3 (Fig. 1, Table S5). The projected population by age and sex shows a larger decline in the population under 65 years than among older adults, with an increase in the size of people aged 65 years and above until the 2050s and then decreasing in the following decades (Fig. 1, Table S5, Figure S3). Comparisons of population changes between prefectures reveal strong variations, with a smaller population decline in urbanized prefectures of higher socio-economic levels, such as Saitama, Chiba, Tokyo, Kanagawa, and Aichi, than less urbanized prefectures (Table S6, Figures S4 and S5).

Heat-related and cold-related mortality and morbidity risks by cause, age, and sex at the country level between 2015 and 2019 are reported in appendix (see Table S7 for specific risk estimates). Non-optimal temperatures showed contrasting patterns of effects on mortality and morbidity, with elevated risks associated with cold temperatures for all-cause mortality as compared to morbidity, and conversely, a higher risk of morbidity in relation to heat. These disparities varied by specific causes but remained consistent across respective age- and sex-subpopulations. There are pronounced disparities in age-specific estimates, particularly for morbidity, with older adults (≥ 65 yr) exhibiting increased susceptibility to cold and younger individuals showing greater sensitivity to heat (Figure S6).

After taking account of both climate and population change scenarios, the temporal change of future excess mortality indicates a common trend of reduced cold-related mortality and increased heat-related excess deaths (Fig. 2, Tables S8 and S9, Figures S7 and S8). Despite the temporal increase in impacts caused by high temperatures, heat-attributable mortality is relatively small compared to the mortality burden attributable to low temperatures, resulting in a net decrease in the total temperature-related mortality rate by specific cause, age, and sex groups (Fig. 2). Total non-optimal temperature-attributable all-cause mortality rate projected in 2010s, 2050s, and 2090s under SSP2-4.5 were 94.29 (44.82, 139.73), 83.69 (38.32, 124.97), and 77.31 (36.84, 114.47) person per 100,000 population, respectively (Table S10). While cold- and heat-related morbidity trends followed similar temporal trends as mortality in terms of attributable risks (Tables S11 and S12, Figures S9 and S10), a net increase in future temperature-attributable all-cause and respiratory morbidity rate by age and sex is projected, driven by greater high temperature-related morbidity than low temperature-related morbidity (Fig. 3, Table S13). All-cause morbidity rate attributable to total non-optimal temperatures among general population was projected to rise substantially from 315.53

(250.91, 371.15) in the 2010s to 345.07 (258.31, 438.66) in the 2050s and 379.62 (271.45, 509.05) persons 100,000 per population in the 2090s under SSP2-4.5. However, the pattern of temperature-attributable morbidity burden due to circulatory causes closely aligns with that of mortality.

Temporal trends in net impacts of non-optimal temperatures on mortality and morbidity were consistent across various subgroups by cause, age, and sex, yet the extent of the burden differed greatly among subgroups, with a more substantial impact observed in people aged 65 years and older and males under all scenarios (Tables S10 and S13). We also observed that the progressive increases in both heat-attributable mortality and morbidity burden are larger in the population aged 65 years and older, and that the total increase is higher in the high-end emissions scenarios than in the low-emissions scenarios (Fig. 4). A similar trend of higher burden in males than in females was found in the comparison of the cause-sex specific groups (Tables S10 and S13).

Prefecture-specific mortality and morbidity burden attributable to non-optimal temperatures under different scenarios are consistent with country-level estimates, consistently showing a decrease in cold-related burden and an increased heat-attributed burden for both endpoints across causes (Tables S14–S16). However, comparison between prefectures reveals strong geographical differences. Under SSP2-4.5, total temperature-attributable all-cause mortality burden in the 2090s ranged from 42.40 (95% eCI: 0.33, 82.33) persons per 100,000 population in Osaka prefecture to 186.41 (95% eCI: 90.01, 273.52) in Akita prefecture, and all-cause morbidity rate varied from 213.12 (95% eCI: –44.39, 450.39) in Ishikawa prefecture to 551.88 (95% eCI: 288.24, 795.16) persons per 100,000 population in Aomori prefecture (Tables S14–S16, Figure S11). Moreover, spatial differences are observed for temporal changes of non-optimal temperature attributable mortality and morbidity rate, with large variations particularly for heat-attributable burden. Fold changes in point estimates of mortality and morbidity rates attributable to high temperatures during the 2090s, relative to the 2010s, at the prefecture level for the general population under SSP2-4.5 are presented in Fig. 5. The most significant increases in mortality and morbidity burden due to high temperatures are generally observed in prefectures such as Hokkaido and Aomori, which are expected to have a large increase in projected temperature, as well as in prefectures with small populations but also larger declines in size, such as Aomori, Akita, Yamanashi, Wakayama, and Kochi (Fig. 5, Tables S14–S16).

We also present results for future temperature-attributable mortality and morbidity under climate change scenarios assuming a constant population (Tables S17 and S18). Projections not accounting for population change had a higher mortality and morbidity

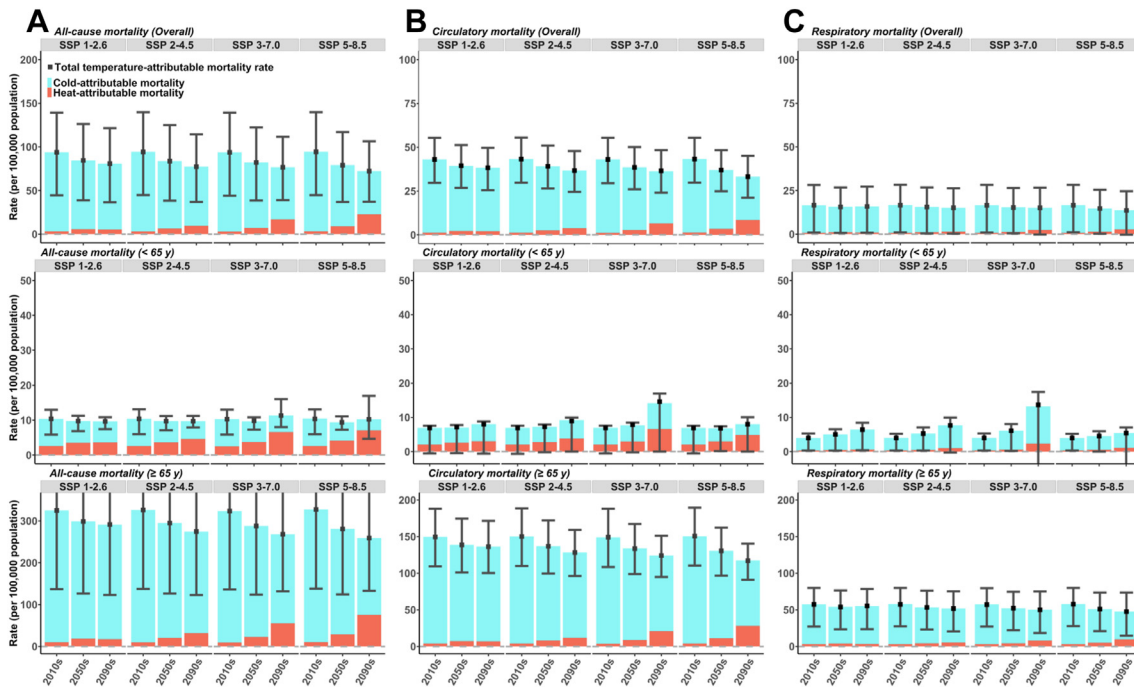


Fig. 2: Temporal trends in non-optimal temperature-attributable excess mortality rate (per 100,000 population) by cause and age groups under alternative climate and population change scenarios during future period. Please note that the scale of each figure is distinct. The vertical lines are 95% empirical confidence intervals (eCIs) for the total temperature-attributable mortality rate. Corresponding numeric data are presented in [Table S10](#).

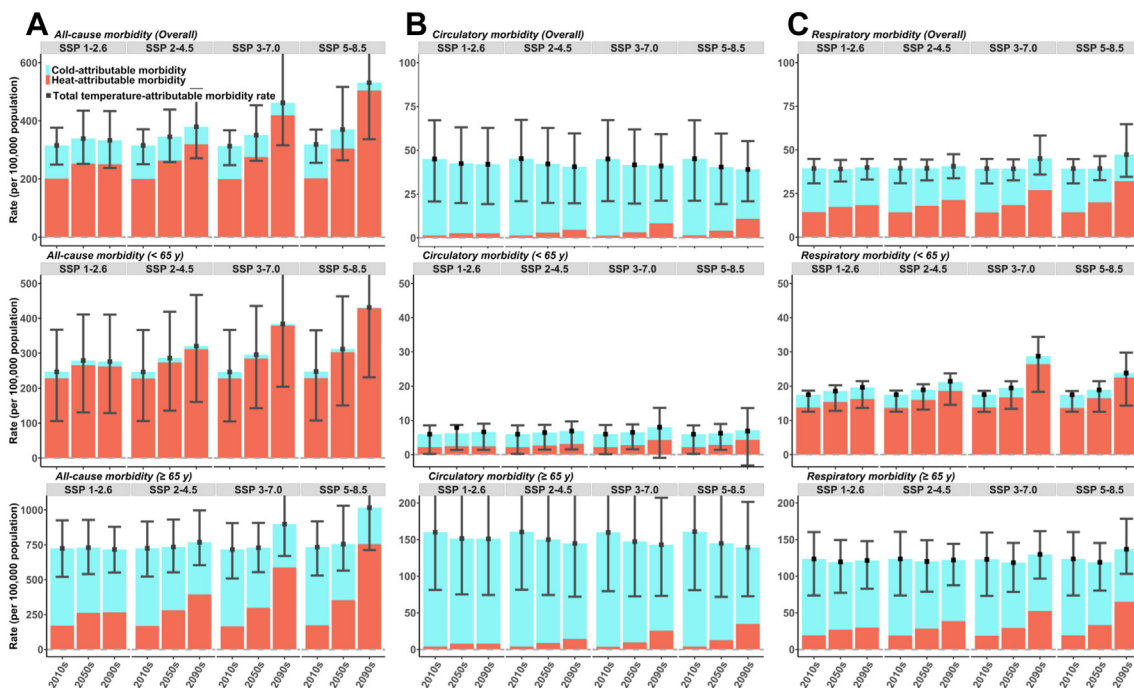


Fig. 3: Temporal trends in non-optimal temperature-attributable morbidity rate (per 100,000 population) by cause and age groups under alternative climate and population change scenarios during future period. Please note that the scale of each figure is distinct. The vertical lines are 95% empirical confidence intervals (eCIs) for the total temperature-attributable morbidity rate. Corresponding numeric data are presented in [Table S13](#).

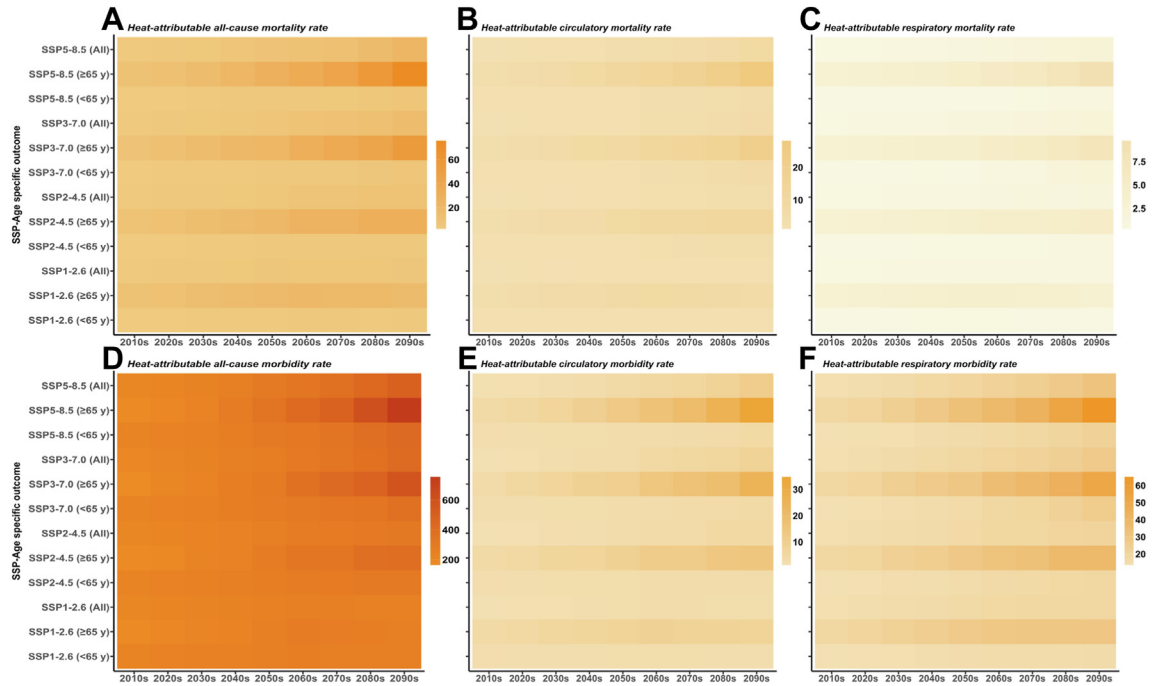


Fig. 4: Decadal trends of heat-attributable morbidity and mortality rate (per 100,000 population) by cause and age groups at country level under alternative climate and population change scenarios. Please note that the scale of each figure is distinct. Corresponding numeric data are presented in [Tables S10](#) and [S13](#).

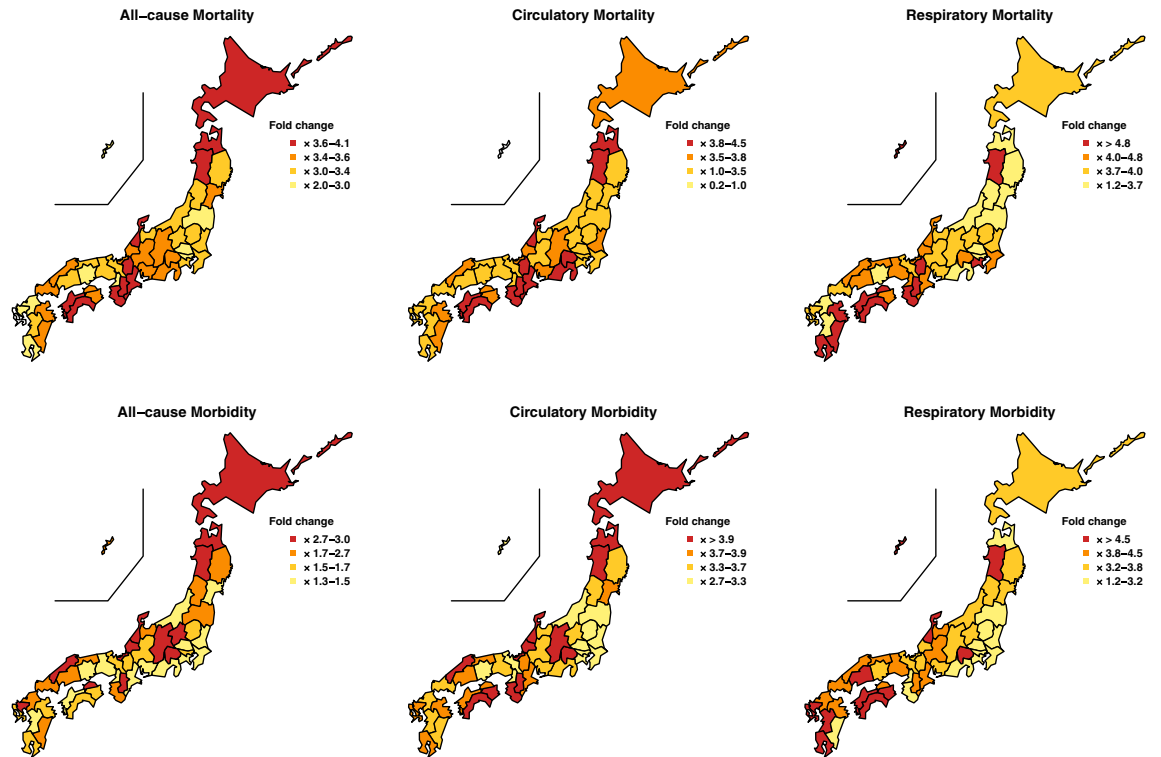


Fig. 5: Fold changes in point estimates of heat-attributable mortality and morbidity rate by causes in general population for 2090–99 compared to 2010–19 under SSP2-4.5 and corresponding population scenario for 47 prefectures in Japan. Please note that the scale of each map is distinct. Corresponding numeric data are presented in [Tables S14–S16](#).

rate attributable to cold temperatures, and a lower morbidity burden attributable to hot temperatures (Table S19). Our projections showed that future temperature attributable mortality and morbidity burden would decrease considerably under the assumption of regularly shifted MMTs, albeit with wide confidence intervals (Tables S20 and S21).

Discussion

In this nationwide modelling study, we applied multiple combinations of climate change and population change scenarios to project the future burden of temperature-attributable mortality and morbidity simultaneously in Japan from 2010 to 2099, at both prefectural and national levels. Differences in susceptibility by cause, age, and sex, and regional disparities were further explored. The results showed that non-optimal temperature attributable mortality burden was projected to decrease slightly, driven by greater low temperature-related mortality than high temperatures-related. In contrast, morbidity patterns revealed that high temperatures contributed more to morbidity than low temperatures, leading to increased burden over time. These patterns persisted across different subgroups, with a higher burden observed among those aged 65 years and older and among males, particularly due to high temperatures. Spatial variations were notable for both mortality and morbidity burdens attributable to non-optimal temperatures, along with their temporal changes.

Our results are largely consistent with previous projections of mortality or morbidity linked to non-optimal temperatures, suggesting a reduction in the cold-related impact and an increase in the heat-related impact, although extant findings have often been limited to the assumption of a constant population.^{18,36,46,47} Moreover, we found that the net impact, in the dynamic balance of the diminishing cold component and the progressively more important heat component, seems dependent on the specific health endpoint and appears more pronounced on morbidity. In particular, the variation of data quality, study design and analytical methods, with alternative effect estimates, modelling and assumption choices, makes it difficult to quantitatively compare the existing projection results on fatal and non-fatal impacts and to draw a comprehensive picture of future non-optimal temperature attributable mortality and morbidity burden. Three previous studies have projected temperature-related mortality and morbidity, but comparability is limited due to differences in exposure metrics, such as the use of maximum temperature during warm season to project heat-related impacts only,² and variations in diseases categories, particularly for infectious diseases,¹² leaving only one study directly comparable to our research. The contrasting net impacts observed in our research align with findings from a study in Rhode Island and Boston, United States. That study, assuming a constant

population, reported a projected increase in temperature-related emergency department visits but fewer temperature-related mortality due to all causes.⁴ In our study, we applied an advanced and well-tested statistical framework, using a unified methodology for both endpoints across all prefectures. We also accounted for combined climate and population change scenarios to provide a comprehensive overview of population susceptibility and geographical differences. Possible explanations for the observed contrasting patterns between temperature-mortality and temperature-morbidity associations in Japan has been previously discussed.⁹ These include differences in disease distribution, with morbidity reflecting less severe, more acute responses to non-optimal temperatures captured earlier by emergency system, while mortality might be influenced by chronic conditions.

In light of the dual challenges posed by global warming and world population aging, emerging studies have projected the combined impacts of warmer climate and demographic changes and reported that population aging may result in a higher heat-related mortality burden than climate-focused estimates.^{13,21,48–52} However, this exacerbated heat effect by future demographics is mostly conducted in an expanding and aging population, and results are often not shown simultaneously before and after accounting for population aging.^{14,52–54} Very little has reported the integrated impacts of warmer climate in a shrinking and aging population as accelerated aging in our case.⁴⁹ Some prior work has been done to project the temperature-related health burden with age-specific estimates,^{14,48–52,55} but little with cause- or sex-specific projections.^{14,15,56} In our study, strong differences were found for comparisons between cause-age and cause-sex specific estimates obtained from exposure–response relationships, particularly for morbidity. Older adults exhibited higher risks of cold-related morbidity due to all causes and circulatory diseases, whereas population younger than 65 years showed a higher risk of heat-related morbidity due to all-cause and respiratory diseases (Table S7). Possible explanations for the observed differences between subgroups during the baseline period have been discussed in the previous investigation.⁹ After considering prefecture-specific population projections, a higher burden was consistently observed for all investigated outcomes among older adults than people younger than 65 yr, especially due to high temperatures. When keeping the population size and structure constant to the current period, the increase in heat attributable burden and the decrease in cold-related impacts will remain, but to a smaller extent. Our findings suggest that population aging plays a role in exacerbating climate-related mortality and morbidity, amplifying the increase in future heat burden and attenuating the decrease in cold-related burden.²⁶ The projected mortality and morbidity burdens from combined climate

and demographic changes are also higher among males than females in the Japanese population. These findings can inform public health intervention policies to ensure that vulnerable populations are protected from non-optimal temperatures, especially heat exposure. This may involve establishing surveillance networks to ensure the safety of homebound older adults and providing passive cooling for outdoor workers.

Geographical differences in temperature-related health burdens across prefectures provide valuable insights for understanding of future trajectories at the prefecture level, as these trajectories are characterized by different climates, socioeconomics, and demographics. The greatest increase in the fold change in mortality and morbidity burden was observed in prefectures characterized by greater increases in mean temperature and larger declines in population; this observation requires further investigation to quantify the contribution of temperature and population change to the observed burden changes in future studies. Therefore, our choice of the prefecture as the unit for modeling is critical for tailoring local adaptation planning and precise interventions, including strengthening infrastructure and public health services, to effectively address disparities.¹⁴

Under the assumption that the future threshold would gradually increase to keep the pace with the rise in temperatures, as justified by self-historical data over four decades, we observe a substantial reduction of both cold- and heat-related impacts. This reduction, especially over the longer term, highlights the importance of ongoing public policy efforts aimed at continued adaptation. The potential to adapt is supported by a growing body of evidence both using the data in areas of geographically different climates and long-term data over decades, showing that populations throughout the world are becoming less sensitive to their local high temperatures.^{10,11,57} Thus, the omission of accounting for such declined susceptibility to non-optimal temperatures in the future might overestimate projected impacts of climate change.⁴⁵ A limited number of studies have explored future temperature-related mortality by incorporating tradeoffs among increasing temperatures, population dynamics, and human adaptation, adding adjustments in the observed exposure-response curves (shifted thresholds and/or changed slopes or borrowed curves from comparable cities).^{48,54,55,58–60} Nevertheless, these attempts relied mostly on liberal assumptions regarding the extent to which the population will adapt to future climates. Few adaptation modeling applications were justified with reference to self-empirical evidence.^{42,53,54} We did not consider concurrent alterations in slopes to avoid introducing greater uncertainty into the model because the observed changes for cold effect are irregular, and it is a challenge to take into account the influence of socioeconomic, technological (such as air conditioning), and behavioral drivers previously

identified for cold- or heat-related susceptibility changes in Japan.^{10,61,62}

Our findings should be interpreted with caution due to several assumptions and limitations. First, this work outlines possible future climatic impacts within a range of hypothetical scenarios rather than making predictions or forecasts of future excess mortality and morbidity. Considerable uncertainty arises from variations in climate modelling, extended time scales, and the estimation of the exposure-response function, especially regarding subpopulations. The omission of external factors that could modify the exposure-response relationship, such as greenness, may also influence the projections of temperature-attributable health burdens.^{14,63} Second, it is important to acknowledge that this morbidity dataset may not encompass all categories of morbidity cases. Our data is obtained from cases using emergency ambulance services, with a large proportion of cases leading to inpatient visits, hospitalizations, and emergency room admissions, and only a small fraction of these cases results in deaths. Nevertheless, it serves as a sensitive indicator for morbidity and effectively captures the most acute and unplanned cases.⁹ In our study, we found that compared with the MMT (88th percentile, 26.7 °C), the risks of circulatory EAD associated with cold (1st percentile, –1.4 °C) and heat (99th percentile, 30.6 °C) were 1.61 (1.50, 1.73) and 1.14 (1.10, 1.18), respectively. However, when it comes to severe conditions, for example, hospitalization, the magnitude of the temperature impact might differ. Another local study has investigated the short-term effects of ambient temperature on hospital admissions due to cardiovascular diseases during 2011 and 2018.⁶⁴ They found that cold temperatures significantly increased the risk of total cardiovascular hospital admissions in 47 prefectures in Japan. The cumulative risk for cold (5th percentile, 1.7 °C) was 1.23 (1.20, 1.26) compared with MMT (98th percentile, 29.9 °C). Whereas no heat effect was observed. In addition, a study in Taiwan utilized emergency room and outpatient visit as the morbidity indicators to investigate the effects of temperature on circulatory diseases, both revealed higher risks associated with cold than heat.⁶ Specifically, emergency room visits showed a higher cold-related risk than outpatient visits [cold-RR 1.41 (1.35, 1.48) and heat-RR 1.02 (1.00, 1.03) for emergency room; cold-RR 1.06 (1.04, 1.09) and heat-RR 1.01 (0.98, 1.03) for outpatient visits]. Hence, previous evidence using different morbidity metrics is largely consistent with our results for emergency ambulance dispatch; but further projection studies using alternative morbidity indicators are warranted for comparison with our findings to gain a comprehensive understanding of temperature-related morbidity impacts. Third, we did not incorporate changes in the rate of mortality and morbidity in the projection because the mortality and morbidity rate projections by cause were not available at prefecture level. Fourth, it is implicit that

we modelled multiplicative interactions rather than additive interactions when conducting the subgroup analysis stratified by sex and age groups. We acknowledge that the latter is also important for our study hypothesis, but it brings methodological complexities that are beyond the scope of this paper. For example, it is difficult to generate RRs in subgroups without heat exposure to assess the additive interaction of two exposures of interest (heat, sex) on the outcome (mortality).⁶⁵ Fifth, our adaptation assumption of a constant pace of adaptation neglected the overall limits to human adaptation.⁴⁵ For example, the observed large reduction of heat-related mortality resulted from the swift proliferation of air conditioning in the past decades would no longer be expected.⁶⁴ In addition, future warming might also outpace the ability to adapt.⁶⁶ The accelerated warming is projected to lead to more frequent, persistent, and life-threatening extreme weather events, along with an exacerbated urban heat island effect that human adaptation cannot keep up with.^{67–70} A caveat that exists in the adaptation modelling for temperature-related morbidity is that it has not been considered or justified in previous works because historical datasets are generally not readily available over a sufficient temporal resolution (spanning several decades). In our initial endeavor, we address this challenge in a straightforward way by adopting a similar adaptation assumption used in modeling temperature associated mortality. Because the selection of adaptation scenarios substantially affects projected climate change impacts, better understanding of both cold and heat adaptation for different endpoints is necessary to improve projections, which is beyond the scope of this study. Last, it is worth noting that our findings can only be generalized to analogous countries or regions characterized by temperate climates and with similar future variations of temperature changes. However, serving as an iconic example of a developed society experiencing an accelerated aging process, our results provide valuable insights for countries or regions elsewhere in the world facing the dual challenges related to climate change and population aging. The large sample size and its representativeness also enhance the generalizability of the study.

In summary, this study offers a comprehensive mapping of climate change impacts on all-cause and cause-specific mortality as well as morbidity, focusing on susceptible population subgroups at local and national levels, considering alternative scenarios of global warming and demographic changes. Three key results deserved highlighting. First, there is a divergence in impact between mortality and morbidity, with cold-attributable mortality and heat-attributable morbidity burden higher across most studied causes in the general population. Second, we observed a higher impact on mortality and morbidity burdens, with greater temporal increases due to heat, among older adults and males. Third, the impact varies across prefectures, with

populations experiencing higher warming levels and, in some cases, larger reduction in population size expected to bear a heavier burden. This systematic perspective on the associated mortality and morbidity burdens offered can inform ongoing planning for mitigation and adaptation. The distinct patterns between mortality and morbidity may help in early health risk preparedness and resource allocation for managing medical services. This evidence enables better preparations tailored to specific disease categories across inpatient, outpatient, and emergency care settings. Additionally, it also contributes to the development and implementation of susceptibility-targeted interventions and coordinated local climate and public health policies.

Contributors

LY, MH, and LM designed the study. LY coordinated the work and took lead in implementing the analysis and drafting the manuscript. YH, KU, KO, and CFSN provided observed weather, mortality, and morbidity data. PLCC provided temperature projection data and assisted in reviewing parts of the R code. MH, LM, AM-VC, AT, KO, CFSN and PLCC provided substantial scientific input in the interpretation of results through early circulation of the analysis results. All authors contributed to the revisions and approbation of the manuscript. MH was responsible for the decision to submit the manuscript after consultation with all listed authors. All authors have seen and approved the final publication.

Data sharing statement

This research used data obtained from the Ministry of Health, Labor and Welfare of Japan, and the Ministry of Internal Affairs and Communications of Japan. Due to legal restrictions, sharing of the original data is prohibited to protect confidentiality.

Editor note

The Lancet Group takes a neutral position with respect to territorial claims in published maps and institutional affiliations.

Declaration of interests

We declare no competing interests.

Acknowledgements

MH was supported by the Japan Science and Technology Agency (JST) as part of SICORP (JPMJSC20E4), and the Environment Research and Technology Development Funds (JPMEERF23S21120 and JPMEERF20231007) of the Environmental Restoration and Conservation Agency provided by Ministry of the Environment of Japan. LY was supported by JST SPRING, Grant Number JPMJSP2108. AT was supported by JSPS KAKENHI Grant Number 24K13527.

Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.lanwpc.2024.101214>.

References

- Huang C, Barnett AG, Wang X, et al. Projecting future heat-related mortality under climate change scenarios: a systematic review. *Environ Health Perspect.* 2011;119(12):1681–1690. <https://doi.org/10.1289/ehp.1103456>.
- Kingsley SL, Eliot MN, Gold J, et al. Current and projected heat-related morbidity and mortality in Rhode Island. *Environ Health Perspect.* 2016;124(4):460–467. <https://doi.org/10.1289/ehp.1408826>.
- Sanderson M, Arbutnott K, Kovats S, et al. The use of climate information to estimate future mortality from high ambient temperature: a systematic literature review. *PLoS One.* 2017;12(7):e0180369. <https://doi.org/10.1371/journal.pone.0180369>.

- 4 Weinberger KR, Kirwa K, Eliot MN, et al. Projected changes in temperature-related morbidity and mortality in southern new England. *Epidemiology*. 2018;29(4):473–481. <https://doi.org/10.1097/EDE.0000000000000825>.
- 5 Kovats RS. Contrasting patterns of mortality and hospital admissions during hot weather and heat waves in Greater London, UK. *Occup Environ Med*. 2004;61(11):893–898. <https://doi.org/10.1136/oem.2003.012047>.
- 6 Lin YK, Sung FC, Honda Y, et al. Comparative assessments of mortality from and morbidity of circulatory diseases in association with extreme temperatures. *Sci Total Environ*. 2020;723:138012. <https://doi.org/10.1016/j.scitotenv.2020.138012>.
- 7 Iñiguez C, Royé D, Tobias A. Contrasting patterns of temperature related mortality and hospitalization by cardiovascular and respiratory diseases in 52 Spanish cities. *Environ Res*. 2021;192:110191. <https://doi.org/10.1016/j.envres.2020.110191>.
- 8 Hanzlíková H, Plavcová E, Kynčl J, et al. Contrasting patterns of hot spell effects on morbidity and mortality for cardiovascular diseases in the Czech Republic, 1994–2009. *Int J Biometeorol*. 2015;59(11):1673–1684. <https://doi.org/10.1007/s00484-015-0974-1>.
- 9 Yuan L, Madaniyazi L, Vicedo-Cabrera AM, et al. A nationwide comparative analysis of temperature-related mortality and morbidity in Japan. *Environ Health Perspect*. 2023;131:127008. <https://doi.org/10.1289/EHP12854>.
- 10 Chung Y, Yang D, Gasparrini A, et al. Changing susceptibility to non-optimum temperatures in Japan, 1972–2012: the role of climate, demographic, and socioeconomic factors. *Environ Health Perspect*. 2018;126(5):057002. <https://doi.org/10.1289/EHP2546>.
- 11 Tobias A, Hashizume M, Honda Y, et al. Geographical variations of the minimum mortality temperature at a global scale: a multi-country study. *Environ Epidemiol*. 2021;5(5):e169. <https://doi.org/10.1097/EE9.0000000000000169>.
- 12 Chua PLC, Ng CFS, Madaniyazi L, et al. Projecting temperature-attributable mortality and hospital admissions due to enteric infections in the Philippines. *Environ Health Perspect*. 2022;130(2):027011. <https://doi.org/10.1289/EHP9324>.
- 13 De Schrijver E, Sivaraj S, Raible CC, et al. Nationwide projections of heat- and cold-related mortality impacts under various climate change and population development scenarios in Switzerland. *Environ Res Lett*. 2023;18(9):094010. <https://doi.org/10.1088/1748-9326/acc7e1>.
- 14 Hebbert C, Gosselin P, Chen K, et al. Future temperature-related excess mortality under climate change and population aging scenarios in Canada. *Can J Public Health*. 2023;114(5):726–736. <https://doi.org/10.17269/s41997-023-00782-5>.
- 15 Li T, Ban J, Horton RM, et al. Heat-related mortality projections for cardiovascular and respiratory disease under the changing climate in Beijing, China. *Sci Rep*. 2015;5(1):11441. <https://doi.org/10.1038/srep11441>.
- 16 Guo Y, Li S, Liu DL, et al. Projecting future temperature-related mortality in three largest Australian cities. *Environ Pollut*. 2016;208:66–73. <https://doi.org/10.1016/j.envpol.2015.09.041>.
- 17 Vicedo-Cabrera AM, Guo Y, Sera F, et al. Temperature-related mortality impacts under and beyond Paris Agreement climate change scenarios. *Climatic Change*. 2018;150(3-4):391–402. <https://doi.org/10.1007/s10584-018-2274-3>.
- 18 Lay CR, Sarofim MC, Vodonos Zilberg A, et al. City-level vulnerability to temperature-related mortality in the USA and future projections: a geographically clustered meta-regression. *Lancet Planet Health*. 2021;5(6):e338–e346. [https://doi.org/10.1016/S2542-5196\(21\)00058-9](https://doi.org/10.1016/S2542-5196(21)00058-9).
- 19 Silveira IH, Cortes TR, De Oliveira BFA, Junger WL. Projections of excess cardiovascular mortality related to temperature under different climate change scenarios and regionalized climate model simulations in Brazilian cities. *Environ Res*. 2021;197:110995. <https://doi.org/10.1016/j.envres.2021.110995>.
- 20 Alahmad B, Vicedo-Cabrera AM, Chen K, et al. Climate change and health in Kuwait: temperature and mortality projections under different climatic scenarios. *Environ Res Lett*. 2022;17(7):074001. <https://doi.org/10.1088/1748-9326/ac7601>.
- 21 Chen K, Vicedo-Cabrera AM, Dubrow R. Projections of ambient temperature- and air pollution-related mortality burden under combined climate change and population aging scenarios: a review. *Curr Envir Health Rpt*. 2020;7(3):243–255. <https://doi.org/10.1007/s40572-020-00281-6>.
- 22 Cole R, Hajat S, Murage P, et al. The contribution of demographic changes to future heat-related health burdens under climate change scenarios. *Environ Int*. 2023;173:107836. <https://doi.org/10.1016/j.envint.2023.107836>.
- 23 Chen H, Matsuhashi K, Takahashi K, et al. Adapting global shared socio-economic pathways for national scenarios in Japan. *Sustain Sci*. 2020;15(3):985–1000. <https://doi.org/10.1007/s11625-019-00780-y>.
- 24 NIES. Japan shared socioeconomic pathways: population projections. <https://adaptation-platform.nies.go.jp/socioeconomic/population.html>; 2020.
- 25 Honjo K, Gomi K, Kanamori Y, et al. Long-term projections of economic growth in the 47 prefectures of Japan: an application of Japan shared socioeconomic pathways. *Heliyon*. 2021;7(3):e06412. <https://doi.org/10.1016/j.heliyon.2021.e06412>.
- 26 De Schrijver E, Bundo M, Ragetli MS, et al. Nationwide analysis of the heat- and cold-related mortality trends in Switzerland between 1969 and 2017: the role of population aging. *Environ Health Perspect*. 2022;130(3):037001. <https://doi.org/10.1289/EHP9835>.
- 27 Xing Q, Sun Z, Tao Y, et al. Projections of future temperature-related cardiovascular mortality under climate change, urbanization and population aging in Beijing, China. *Environ Int*. 2022;163:107231. <https://doi.org/10.1016/j.envint.2022.107231>.
- 28 Kc S, Lutz W. The human core of the shared socioeconomic pathways: population scenarios by age, sex and level of education for all countries to 2100. *Global Environ Change*. 2017;42:181–192. <https://doi.org/10.1016/j.gloenvcha.2014.06.004>.
- 29 Lange S, Büchner M. *ISIMIP3b bias-adjusted atmospheric climate input data*. 2021. <https://doi.org/10.48364/ISIMIP.842396.1>.
- 30 Frieler K, Volkholz J, Lange S, et al. Scenario set-up and forcing data for impact model evaluation and impact attribution within the third round of the inter-sectoral model Intercomparison project (ISIMIP3a). *Geosci Model Dev*. 2024;17:1–51. <https://doi.org/10.5194/gmd-17-1-2024>.
- 31 O'Neill BC, Kriegler E, Ebi KL, et al. The roads ahead: narratives for shared socioeconomic pathways describing world futures in the 21st century. *Global Environ Change*. 2017;42:169–180. <https://doi.org/10.1016/j.gloenvcha.2015.01.004>.
- 32 IPCC. Summary for Policymakers. In: Core Writing Team, Lee H, Romero J, eds. *Climate Change 2023: Synthesis Report. Contribution of Working Groups I, II and III to the Sixth Assessment Report of the Intergovernmental Panel on Climate Change*. Geneva, Switzerland: IPCC; 2023:1–34. <https://doi.org/10.59327/IPCC/AR6-9789291691647.001>.
- 33 Hempel S, Frieler K, Warszawski L, et al. A trend-preserving bias correction – the ISI-MIP approach. *Earth Syst Dynam*. 2013;4(2):219–236. <https://doi.org/10.5194/esd-4-219-2013>.
- 34 NIES. *Population scenarios by shared socioeconomic pathways (SSP) for Japan*. V.2. NIES; 2021. <https://adaptation-platform.nies.go.jp/socioeconomic/population.html>.
- 35 Oka K, Honda Y, Phung VLH, Hijioka Y. Prediction of climate change impacts on heatstroke cases in Japan's 47 prefectures with the effect of long-term heat adaptation. *Environ Res*. 2023;232:116390. <https://doi.org/10.1016/j.envres.2023.116390>.
- 36 Gasparrini A, Guo Y, Sera F, et al. Projections of temperature-related excess mortality under climate change scenarios. *Lancet Planet Health*. 2017;1(9):e360–e367. [https://doi.org/10.1016/S2542-5196\(17\)30156-0](https://doi.org/10.1016/S2542-5196(17)30156-0).
- 37 Vicedo-Cabrera AM, Sera F, Gasparrini A. Hands-on tutorial on a modeling framework for projections of climate change impacts on health. *Epidemiology*. 2019;30(3):321–329. <https://doi.org/10.1097/EDE.0000000000000982>.
- 38 Gasparrini A, Armstrong B, Kenward MG. Multivariate meta-analysis for non-linear and other multi-parameter associations. *Stat Med*. 2012;31(29):3821–3839. <https://doi.org/10.1002/sim.5471>.
- 39 Sera F, Gasparrini A. Extended two-stage designs for environmental research. *Environ Health*. 2022;21(1):41. <https://doi.org/10.1186/s12940-022-00853-z>.
- 40 Gasparrini A, Guo Y, Hashizume M, et al. Mortality risk attributable to high and low ambient temperature: a multicountry observational study. *Lancet*. 2015;386(9991):369–375. [https://doi.org/10.1016/S0140-6736\(14\)62114-0](https://doi.org/10.1016/S0140-6736(14)62114-0).
- 41 Gasparrini A, Leone M. Attributable risk from distributed lag models. *BMC Med Res Methodol*. 2014;14(1):55. <https://doi.org/10.1186/1471-2288-14-55>.
- 42 Huber V, Peña Ortiz C, Gallego Puyol D, et al. Evidence of rapid adaptation integrated into projections of temperature-related excess mortality. *Environ Res Lett*. 2022;17(4):044075. <https://doi.org/10.1088/1748-9326/ac5dee>.
- 43 Lim SS, Vos T, Flaxman AD, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the global burden of disease study 2010.

- Lancet*. 2012;380(9859):2224–2260. [https://doi.org/10.1016/S0140-6736\(12\)61766-8](https://doi.org/10.1016/S0140-6736(12)61766-8).
- 44 Honda Y, Kondo M, McGregor G, et al. Heat-related mortality risk model for climate change impact projection. *Environ Health Prev Med*. 2014;19(1):56–63. <https://doi.org/10.1007/s12199-013-0354-6>.
 - 45 Gosling SN, Hondula DM, Bunker A, et al. Adaptation to climate change: a comparative analysis of modeling methods for heat-related mortality. *Environ Health Perspect*. 2017;125(8):087008. <https://doi.org/10.1289/EHP634>.
 - 46 Martínez-Solanas E, Quijal-Zamorano M, Achebak H, et al. Projections of temperature-attributable mortality in Europe: a time series analysis of 147 contiguous regions in 16 countries. *Lancet Planet Health*. 2021;5(7):e446–e454. [https://doi.org/10.1016/S2542-5196\(21\)00150-9](https://doi.org/10.1016/S2542-5196(21)00150-9).
 - 47 Liu J, Lv C, Zheng J, et al. The impact of non-optimum temperatures, heatwaves and cold spells on out-of-hospital cardiac arrest onset in a changing climate in China: a multi-center, time-stratified, case-crossover study. *Lancet Reg Health West Pac*. 2023;36:100778. <https://doi.org/10.1016/j.lanwpc.2023.100778>.
 - 48 Li T, Horton RM, Bader DA, et al. Aging will amplify the heat-related mortality risk under a changing climate: projection for the elderly in Beijing, China. *Sci Rep*. 2016;6(1):28161. <https://doi.org/10.1038/srep28161>.
 - 49 Lee JY, Kim H. Projection of future temperature-related mortality due to climate and demographic changes. *Environ Int*. 2016;94:489–494. <https://doi.org/10.1016/j.envint.2016.06.007>.
 - 50 Liu T, Ren Z, Zhang Y, et al. Modification effects of population expansion, ageing, and adaptation on heat-related mortality risks under different climate change scenarios in Guangzhou, China. *Int J Environ Res Public Health*. 2019;16(3):376. <https://doi.org/10.3390/ijerph16030376>.
 - 51 Jenkins K, Kennedy-Asser A, Andrews O, Lo YTE. Updated projections of UK heat-related mortality using policy-relevant global warming levels and socio-economic scenarios. *Environ Res Lett*. 2022;17(11):114036. <https://doi.org/10.1088/1748-9326/ac9cf3>.
 - 52 Sharma A, Lin YK, Chen CC, et al. Projections of temperature-associated mortality risks under the changing climate in an ageing society. *Public Health*. 2023;221:23–30. <https://doi.org/10.1016/j.puhe.2023.05.017>.
 - 53 Petkova EP, Vink JK, Horton RM, et al. Towards more comprehensive projections of urban heat-related mortality: estimates for New York city under multiple population, adaptation, and climate scenarios. *Environ Health Perspect*. 2017;125(1):47–55. <https://doi.org/10.1289/EHP166>.
 - 54 Rai M, Breitner S, Wolf K, et al. Future temperature-related mortality considering physiological and socioeconomic adaptation: a modelling framework. *Lancet Planet Health*. 2022;6(10):e784–e792. [https://doi.org/10.1016/S2542-5196\(22\)00195-4](https://doi.org/10.1016/S2542-5196(22)00195-4).
 - 55 Lee J, Dessler AE. Future temperature-related deaths in the U.S.: the impact of climate change, demographics, and adaptation. *Geohealth*. 2023;7(8):e2023GH000799. <https://doi.org/10.1029/2023GH000799>.
 - 56 Gu S, Zhang L, Sun S, et al. Projections of temperature-related cause-specific mortality under climate change scenarios in a coastal city of China. *Environ Int*. 2020;143:105889. <https://doi.org/10.1016/j.envint.2020.105889>.
 - 57 Gasparrini A, Guo Y, Hashizume M, et al. Temporal variation in heat–mortality associations: a multicountry study. *Environ Health Perspect*. 2015;123(11):1200–1207. <https://doi.org/10.1289/ehp.1409070>.
 - 58 Lee J, Lee WS, Ebi K, Kim H. Temperature-related summer mortality under multiple climate, population, and adaptation scenarios. *Int J Environ Res Public Health*. 2019;16(6):1026. <https://doi.org/10.3390/ijerph16061026>.
 - 59 Chen CC, Wang YR, Wang YC, et al. Projection of future temperature extremes, related mortality, and adaptation due to climate and population changes in Taiwan. *Sci Total Environ*. 2021;760:143373. <https://doi.org/10.1016/j.scitotenv.2020.143373>.
 - 60 Liu J, Varghese BM, Hansen A, et al. Projection of high temperature-related burden of kidney disease in Australia under different climate change, population and adaptation scenarios: population-based study. *Lancet Reg Health West Pac*. 2023;41:100916. <https://doi.org/10.1016/j.lanwpc.2023.100916>.
 - 61 Sera F, Hashizume M, Honda Y, et al. Air conditioning and heat-related mortality: a multi-country longitudinal study. *Epidemiology*. 2020;31(6):779–787. <https://doi.org/10.1097/EDE.0000000000001241>.
 - 62 Chua PLC, Takane Y, Ng CFS, et al. Net impact of air conditioning on heat-related mortality in Japanese cities. *Environ Int*. 2023;181:108310. <https://doi.org/10.1016/j.envint.2023.108310>.
 - 63 Choi HM, Lee W, Roye D, et al. Effect modification of greenness on the association between heat and mortality: a multi-city multi-country study. *eBioMedicine*. 2022;84:104251. <https://doi.org/10.1016/j.ebiom.2022.104251>.
 - 64 Pan R, Okada A, Yamana H, et al. Association between ambient temperature and cause-specific cardiovascular disease admissions in Japan: a nationwide study. *Environ Res*. 2023;225:115610. <https://doi.org/10.1016/j.envres.2023.115610>.
 - 65 Knol MJ, VanderWeele TJ. Recommendations for presenting analyses of effect modification and interaction. *Int J Epidemiol*. 2012;41:514–520. <https://doi.org/10.1093/ije/dyr218>.
 - 66 Lüthi S, Fairless C, Fischer EM, et al. Rapid increase in the risk of heat-related mortality. *Nat Commun*. 2023;14:4894. <https://doi.org/10.1038/s41467-023-40599-x>.
 - 67 Wang Y, Shi L, Zanobetti A, Schwartz JD. Estimating and projecting the effect of cold waves on mortality in 209 US cities. *Environ Int*. 2016;94:141–149. <https://doi.org/10.1016/j.envint.2016.05.008>.
 - 68 Chen H, Zhao L, Cheng L, et al. Projections of heatwave-attributable mortality under climate change and future population scenarios in China. *Lancet Reg Health West Pac*. 2022;28:100582. <https://doi.org/10.1016/j.lanwpc.2022.100582>.
 - 69 Wedler M, Pinto JG, Hochman A. More frequent, persistent, and deadly heat waves in the 21st century over the Eastern Mediterranean. *Sci Total Environ*. 2023;870:161883. <https://doi.org/10.1016/j.scitotenv.2023.161883>.
 - 70 He C, Yin P, Liu Z, et al. Projections of excess deaths related to cold spells under climate and population change scenarios: a nationwide time series modeling study. *Environ Int*. 2023;178:108034. <https://doi.org/10.1016/j.envint.2023.108034>.