

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

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4 Daisuke Onozuka, PhD^{1,2}, Antonio Gasparri, PhD^{3,4}, Francesco Sera, MSc³, Masahiro

5 Hashizume, MD, PhD⁵, Yasushi Honda, MD, PhD⁶

6

7 ¹ Department of Preventive Medicine and Epidemiologic Informatics, National Cerebral and
8 Cardiovascular Center Research Institute, Osaka, Japan

9 ² Department of Health Communication, Kyushu University Graduate School of Medical
10 Sciences, Fukuoka, Japan

11 ³ Department of Public Health, Environments and Society, London School of Hygiene &
12 Tropical Medicine, London, UK

13 ⁴ Centre for Statistical Methodology, London School of Hygiene & Tropical Medicine, London,
14 UK

15 ⁵ Department of Pediatric Infectious Diseases, Institute of Tropical Medicine, Nagasaki
16 University, Nagasaki, Japan

17 ⁶ Faculty of Health and Sport Sciences, University of Tsukuba, Tsukuba, Japan

18

19 **Address for Correspondence:**

20 Daisuke Onozuka, PhD

21 Department of Preventive Medicine and Epidemiologic Informatics

22 National Cerebral and Cardiovascular Center Research Institute

23 5-7-1 Fujishirodai, Suita, Osaka 565-8565, Japan

24 Tel.: +81-6-6833-5012

25 Fax: +81-6-6872-8091

26 E-mail: onozukad@ncvc.go.jp

27

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32 **Abstract**

33 **Background:** Recent studies have reported associations between global climate change and
34 mortality. However, future projections of temperature-related out-of-hospital cardiac arrest
35 (OHCA) have not been thoroughly evaluated. Thus, we aimed to project temperature-related
36 morbidity for OHCA concomitant with climate change.

37 **Methods:** We collected national registry data on all OHCA cases reported in 2005–2015 from all
38 47 Japanese prefectures. We used a two-stage time series analysis to estimate temperature-
39 OHCA relationships. Time series of current and future daily mean temperature variations were
40 constructed according to four climate change scenarios of representative concentration pathways
41 (RCPs) using five general circulation models. We projected excess morbidity for heat and cold
42 and the net change in 1990–2099 for each climate change scenario using the assumption of no
43 adaptation or population changes.

44 **Results:** During the study period, 739,717 OHCAs of presumed cardiac origin were reported.
45 Net decreases in temperature-related excess morbidity were observed under higher emission
46 scenarios. The net change in 2090–2099 compared with 2010–2019 was -0.8% (95% empirical
47 confidence interval [eCI]: -1.9, 0.1) for a mild emission scenario (RCP2.6), -2.6% (95% eCI: -
48 4.4, -0.8) for a stabilization scenario (RCP4.5), -3.4% (95% eCI: -5.7, -1.0) for a stabilization
49 scenario (RCP6.0), and -4.2% (95% eCI: -8.3, -0.1) for an extreme emission scenario (RCP8.5).

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

54

55

56 INTRODUCTION

57 Climate change is widely recognized as the most significant global health threat of the
58 21st century, and tackling climate change could be the greatest global health opportunity (Watts
59 et al., 2015). The fifth Intergovernmental Panel on Climate Change (IPCC) report indicates that
60 high-end emissions scenarios project increases in global mean temperatures of between 2.6 and
61 4.8°C by the end of the century (Pachauri et al., 2014). While a number of important human
62 diseases have been associated with shifts in climate, a lack of long-term, high-quality data and a
63 significant influence from socio-economic factors has led to some uncertainty in attributing any
64 increase or re-emergence of diseases to climate change (Patz et al., 2005). Recent studies have
65 shown that climate change has the potential to substantially increase temperature-related
66 mortality (Benmarhnia et al., 2014; Gasparrini et al., 2017; Hajat et al., 2014; Lee and Kim,
67 2016). However, the future impact of health threats arising from climate change can differ quite
68 significantly among diseases (Watts et al., 2015), and the impacts of climate change on
69 morbidity has not been thoroughly evaluated.

70 Sudden cardiac arrest is a major contributor to morbidity and mortality in the general
71 population, and accounts for almost 10–20% of all deaths (Field et al., 2010). In particular, out-
72 of-hospital cardiac arrest (OHCA) is characterized by unexpected collapse due to a cardiac
73 disorder (Tian and Qiu, 2017). Although resuscitation rates are generally improving globally,
74 OHCA is a leading global cause of mortality (Nichol et al., 2008; Wissenberg et al., 2013).
75 Coronary artery disease is a key contributor to sudden cardiac arrest (Mozaffarian et al., 2015).
76 However, OHCA is multifactorial and complex in nature (Patz et al., 2005). Several studies that
77 aimed to quantify the burden of OHCA have had difficulty accurately accounting for potential
78 adaptation to climate change over time and place. Meanwhile, OHCA remains a prime and

79 significant cause of death due to cardiovascular diseases. It is therefore paramount to focus on
80 OHCA to improve prediction estimates and to aid in prioritizing mitigation and adaptation
81 policies to climate change in the future.

82 As concerns associated with climate change have increased over the past few decades,
83 there has been emerging evidence supporting a relationship between OHCA and environmental
84 factors such as extreme weather conditions like heat and cold events (Onozuka and Hagihara,
85 2017a; Onozuka and Hagihara, 2017c; Onozuka and Hagihara, 2017e). For example, several
86 studies have shown a positive association between extremely high and low temperatures and
87 OHCA risk (Onozuka and Hagihara, 2017a). Moreover, recent studies have also shown that the
88 majority of temperature-related OHCA burden is attributable to low temperatures, and that the
89 effect of extreme temperatures is substantially lower than that of moderate temperatures
90 (Onozuka and Hagihara, 2017c). These findings suggest that climate change may raise heat-
91 related morbidity, while concomitantly reducing cold-related morbidity. However, future
92 projections of temperature-related excess morbidity due to OHCA according to climate change
93 scenarios have not been studied. Furthermore, the degree to which the anticipated reduction in
94 cold-related morbidity can counter the rise in heat-related morbidity remains to be determined.
95 This data will be important for the development of coordinated and evidence-based climate
96 change and public health methods to prevent climate change-related OHCA.

97 Here, we aimed to project the future impact of climate change on temperature-attributable
98 OHCA morbidity using Japanese national registry data from all OHCA cases reported in 2005–
99 2015 that were assumed to be of cardiac origin.

100

101 **METHODS**

102 **Study design**

103 We used the same study design and statistical framework described in detail elsewhere
104 (Gasparrini et al., 2017; Vicedo-Cabrera et al., 2019). Briefly, we used a two-stage time-series
105 analysis to predict the association between temperature and daily morbidity due to OHCA in all
106 47 Japanese prefectures. Additionally, we acquired daily mean temperature time-series according
107 to climate change scenarios of the four representative concentration pathways (RCPs), RCP2.6,
108 RCP4.5, RCP6.0, and RCP8.5. We merged these data to estimate future projections of excess
109 morbidity attributable to temperature.

110

111 **Ethics approval**

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

116

117 **Data sources**

118 We used national registry data from the FDMA regarding all OHCA cases that were
119 reported from 2005 to 2015 in all 47 Japanese prefectures. According to Japan's Fire Service Act,
120 municipal government-enlisted emergency medical services (EMSs) are provided at around 800
121 fire stations and related dispatch centers across Japan. Given that EMS providers do not have the
122 authority to terminate resuscitation in the field, all EMS-treated OHCA cases are transported to a
123 hospital. EMS personnel summarize each OHCA case in conjunction with the physician in
124 charge according to the standardized Utstein-style reporting guidelines for cardiac arrest

125 (Hagihara et al., 2012). The physician in charge together with the EMS personnel clinically
126 ascertained the cause of cardiac arrest (i.e., presumed cardiac or non-cardiac). All arrests were
127 considered to be of cardiac origin unless the cause was drowning, trauma, drug overdose,
128 exsanguination, asphyxia, or any other obvious non-cardiac cause. Fire stations with dispatch
129 centers in the 47 prefectures send their data to the FDMA, where the data is incorporated into the
130 national registry system on the FDMA database server. According to the Fire Service Act, all
131 OHCA cases must be registered in Japan. The national registry data for OHCA cases is therefore
132 regarded as comprehensive across the country. The FDMA's computer system was used to check
133 and validate the data for consistency (Kitamura et al., 2016). We included all patients that
134 experienced an OHCA of presumed cardiac origin, and we extracted the daily time-series of
135 OHCA cases from the national registry database.

136 We also acquired data on daily mean temperatures from the Japan Meteorological
137 Agency. Data from one weather station positioned in an urban area of the capital city was used as
138 representative data for the region for each prefecture because these were synoptic climatological
139 stations and intended to capture macro-scale weather for each prefecture. Daily mean
140 temperatures were computed as 24-hour averages according to hourly measurements. Daily mean
141 temperature was used as the main exposure index as it is indicative of exposure throughout the
142 day and can be readily interpreted for decision-making purposes (Guo et al., 2011; Guo et al.,
143 2014).

144

145 **Scenario models**

146 We estimated the projections of future temperature-related OHCA under four climate
147 change scenarios using models of climate change and morbidity. First, we acquired time series

148 data for daily mean temperatures according to four climate change scenarios of representative
149 concentration pathways (RCPs) (van Vuuren et al., 2011a). The four RCPs (RCP2.6, RCP4.5,
150 RCP6.0, and RCP8.5) present rising greenhouse gas concentration trajectories: RCP2.6 models a
151 mild emission scenario in which peaks in radiative forcing at $\sim 3 \text{ W/m}^2$ before 2100 and then
152 declines to 2.6 W/m^2 by 2100, RCP4.5 models a stabilization scenario in which total radiative
153 forcing is stabilized shortly after 2100, without overshooting the long-run radiative forcing target
154 level of 4.5 W/m^2 , RCP6 models a stabilization scenario in which total radiative forcing is
155 stabilized shortly after 2100, without overshoot pathway to 6 W/m^2 , by the application of a range
156 of technologies and strategies for reducing greenhouse gas emissions, and RCP8.5 models an
157 extreme emission scenario in which rising radiative forcing pathway leading to 8.5 W/m^2 by
158 2100 (van Vuuren et al., 2011a). The RCPs were generated following collaborations between
159 integrated assessment modelers, climate modelers, terrestrial ecosystem modelers, and emission
160 inventory experts (van Vuuren et al., 2011a). Future projections of daily mean temperatures
161 under each RCP were then developed using general circulation models (GCMs) (Warszawski et
162 al., 2014). GCMs were designed to enable the quantification of representation of historical,
163 current, and projected climate consistent with scenarios of increases in radiative atmospheric
164 forces, summarized by RCPs. The Inter-Sectoral Impact Model Intercomparison Project (ISI-
165 MIP) database includes daily temperature series for each RCP scenario of five GCMs (GFDL-
166 ESM2M (Dunne et al., 2012; Dunne et al., 2013), HadGEM2-ES (Jones et al., 2011), IPSL-
167 CM5A-LR (Mignot and Bony, 2013), MIROC-ESM-CHEM (Watanabe et al., 2011), and
168 NorESMI-M (Bentsen et al., 2013; Iversen et al., 2013)), and these five GCMs were regarded as
169 the representatives of the full range of projections of future climate based on the current existing
170 scientific literature within the fifth phase of the Climate Model Intercomparison Project (CMIP5)

171 models (Taylor et al., 2012; Warszawski et al., 2014). The ISI-MIP database
172 (<https://www.isimip.org/>) contains time series of daily mean temperatures for historical (1960–
173 2005) and projected (2006–2099) periods, which are bias-corrected and downscaled to
174 $0.5^\circ \times 0.5^\circ$ spatial resolution (Warszawski et al., 2014). GCMs were generated by considering
175 the difference in climate change impact at varying levels of global warming according to the four
176 RCPs to produce the highest and lowest end-of-century forcings (Warszawski et al., 2014).
177 When the modelled daily temperature series are applied to exposure-response relationships
178 estimated using observed daily time series for daily mean temperature, deviations between the
179 modelled and observed daily temperature series may produce biased results in the impact
180 projections. Therefore, the modelled daily temperature series were corrected using the bias-
181 correction method, which recalibrated using the monthly mean and the daily variability around
182 the monthly mean of observed daily temperature series (Hempel et al., 2013). We calculated the
183 projected daily time series of OHCA as the mean observed count for each day of the year, and
184 repeated this across the projection period (1990–2099).

185

186 **Statistical analysis**

187 *Estimation of exposure-response relationships*

188 We used two-stage time series analysis to predict the prefecture-specific non-linear lag
189 impact of temperature on OHCA, as described previously (Gasparrini et al., 2016; Onozuka and
190 Hagihara, 2017c; Zhang et al., 2019; Zhang et al., 2017). Briefly, first, we investigated the
191 association between temperature and OHCA in individual prefectures using a time-series quasi-
192 Poisson regression model combined with a distributed lag non-linear model, adjusting for season,
193 long-term trends, and day of the week. We examined lag periods of up to 21 days to consider the

194 delayed impact of low temperatures. Second, we combined prefecture-specific estimates using
195 multivariate meta-regression models to predict the nationwide non-linear temperature-OHCA
196 association. This method has been described in detail elsewhere (Gasparrini et al., 2017; Vicedo-
197 Cabrera et al., 2019).

198

199 *Projection of the effect on morbidity*

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

216 among GCMs. Details of this method were described previously (Gasparrini et al., 2017; Vicedo-
217 Cabrera et al., 2019).

218 For sensitivity analysis, modeling selections were tested by controlling for different
219 degrees of freedom for time trends (6 and 10 degrees of freedom per year), by choosing different
220 lags (14 and 28 days), and by including or excluding different confounding factors (relative
221 humidity, public holiday, and day of the week). All statistical analyses were conducted using R
222 3.5.0 (R Core Team, R Foundation for Statistical Computing, Vienna, Austria), specifically using
223 the *dlnm* and *mvmeta* packages.

224

225 **RESULTS**

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

231 The variation in the mean temperature in the current period (2010–19) and the projected
232 increase at the end of the 21st century (2090–99) in the four RCP scenarios in Japan are shown in
233 Figure 2 and Table 1. We projected a steep rise in mean temperatures under high-end emission
234 scenarios (RCP6.0 and RCP8.5); however, this rise slowed or tended to be reduced after a
235 number of decades under climate change scenarios that assume greenhouse gas mitigation
236 policies (RCP2.6 and RCP4.5) (Figure 2 and Figure S2 in the Supplement). By the end of the
237 21st century, a drop in greenhouse gas emissions may avert warming in Japan, with a mean rise
238 in temperature of 0.6°C (range: 0.4–0.9) under RCP2.6 compared to 4.0°C (range: 3.0–4.9)

239 under RCP8.5. The respective data from each prefecture are shown in Figures S2 and S3 in the
240 Supplement.

241 Projected trends in heat- and cold-related excess morbidity according to three RCPs in
242 Japan are summarized in Figure 3 and Table 1. Our findings showed a common pattern of a
243 reduction in cold-related morbidity and mild rise in excess morbidity due to heat across the
244 scenarios. The projected slopes were steeper under RCP8.5, while the trends were shallower
245 throughout the 21st century under scenarios that assume mitigation strategies. Cold-related
246 excess morbidity is projected to be reduced from 19.9% (95% eCI: -0.1, 33.4) in 2010–2019 to
247 13.8% (95% eCI: -2.5, 25.5) in 2090–2099 under scenarios of intense warming (RCP8.5), and
248 there is a large degree of uncertainty for cold-related morbidity. In contrast, heat-related excess
249 morbidity is projected to rise from 0.4% (95% eCI: 0.1, 0.6) to 2.4% (95% eCI: 0.5, 4.2) across
250 the same period and conditions. The respective data from each prefecture are shown in Figures
251 S4 and S5 in the Supplement.

252 Temporal changes in excess morbidity under three different RCPs in Japan are
253 summarized in Figure 4 and Table 3. There was a marked net reduction in excess morbidity,
254 ranging from -0.8% (95% eCI -1.9, 0.1) under RCP2.6 to -4.2% (95% eCI -8.3, -0.1) under
255 RCP8.5. The respective data from each prefecture are shown in Figure S6 and Tables S2-S5 in
256 the Supplement.

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

259

260 **DISCUSSION**

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

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

283 The net reduction in OHCA as a result of global warming may be explained by several
284 mechanisms. First, increasing temperature due to global warming may reduce health problems
285 related to low temperatures, which can lead to offset the increase in morbidity by high
286 temperatures. A recent study has shown that, although both high and low temperatures are
287 responsible for OHCA burden, most OHCA cases are attributable to low temperatures (Onozuka
288 and Hagihara, 2017c). Regarding low temperature-related health problems, recent studies have
289 indicated that circulatory and coronary heart disease and ST-elevation myocardial infarction
290 (STEMI) mortality is increased with low temperatures (Schwartz et al., 2015). It is possible that
291 low temperatures trigger sympathetic stimulation and a rise in cardiac workload, which could
292 stress a person with severe coronary stenosis and/or advanced heart failure beyond their
293 compensation threshold (Izzo et al., 1990; Schwartz et al., 2015; Wolf et al., 2009). Second, low
294 temperatures may contribute to the cardiovascular stress response by increasing blood viscosity,
295 changing heart rate variability, and impacting inflammatory responses (Keatinge et al., 1986).
296 Low temperature periods have been linked to high excess risk of heart failure, arrhythmia, and
297 atrial fibrillation (Medina-Ramon et al., 2006). Low temperatures raise sympathetic tone, blood
298 pressure, vascular resistance, fibrinogen level, platelet count, some clotting factors, and blood
299 viscosity, which can raise the risk of plaque rupture, thrombosis, and STEMI mortality (Izzo et
300 al., 1990; Schwartz et al., 2015; Wolf et al., 2009). Furthermore, those with reduced vitamin D
301 levels are vulnerable to sudden cardiac death during winter, suggesting that increasing vitamin D
302 levels by adequate sun exposure in the winter months may be significant for decreasing sudden
303 cardiac death (Deo et al., 2011; Drechsler et al., 2010; Giovannucci et al., 2008; Onozuka and
304 Hagihara, 2017b; Onozuka and Hagihara, 2017d). Our findings are therefore physiologically

305 plausible and suggest that climate change according to different levels of future global warming
306 may markedly reduce OHCA.

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

318 Our results have practical implications for refining or adjusting estimates for climate
319 change-related OHCA in future public health policies. Our study projects a largest decrease in
320 net excess OHCA morbidity due to climate change under high-emission scenarios. The majority
321 of the excess morbidity was attributable to low temperatures, while heat was only associated
322 with a small fraction of excess morbidity. Additionally, the reduction in temperature-related net
323 excess morbidity is expected to be significant in scenarios of high greenhouse gas emissions.
324 These findings are important for the development of disease-specific public health policies, and
325 for informing the ongoing international discussion on the health impacts of climate change.

326 There were several limitations in our study. First, while our projections of temperature-
327 OHCA relationships according to future warming scenarios enabled isolation of the effects of

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

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

346

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351

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357 data analysis, data interpretation, or preparation of the manuscript.

358

359 **Author Contributions**

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

365

366 **Competing Interests**

367 The authors declare that they have no competing interests.

368

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510

511 **Figure legends**

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

514

515 **Figure 2.** Decadal temperature trends in Japan by scenario. The graph shows the projected
516 increase in temperature ($^{\circ}\text{C}$, GCM-ensemble average), averaged by decade and climate change
517 scenario, compared to the current period (2010–2019).

518

519 **Figure 3.** Trends in heat-related and cold-related excess morbidity in Japan. The graph shows the
520 excess morbidity by decade attributed to heat and cold under three climate change scenarios
521 (RCP2.6, RCP4.5, and RCP8.5). Estimates are reported as GCM-ensemble mean decadal
522 fractions. The shaded areas represent 95% empirical confidence intervals (eCIs).

523 RCP=representative concentration pathway; GCM=general circulation model.

524

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

530 **Tables**

531 **Table 1.** Heat-related, cold-related, and net excess morbidity (%) with 95% eCI by period and
 532 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)

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

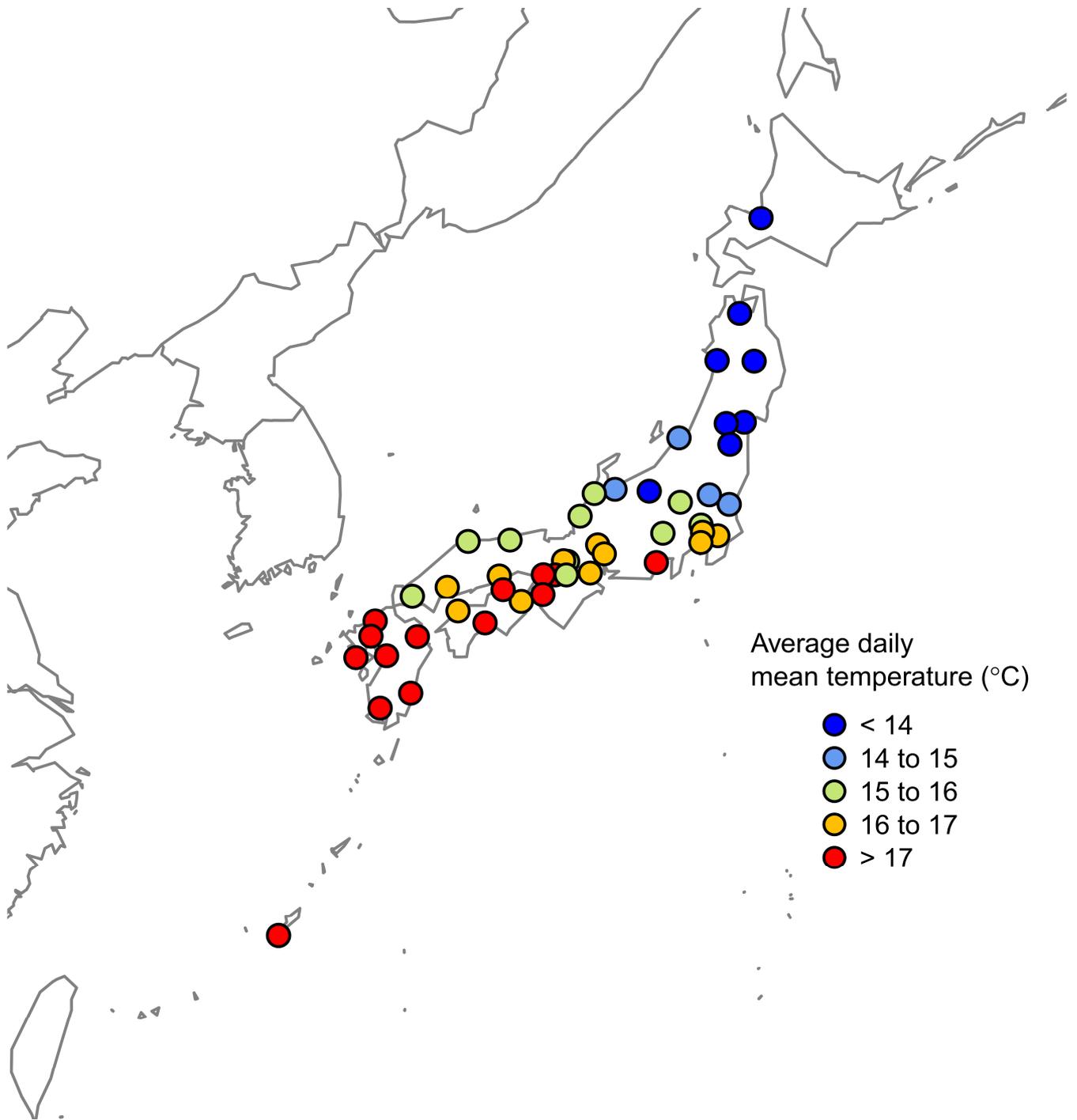


Figure 1

Japan (47 prefectures)

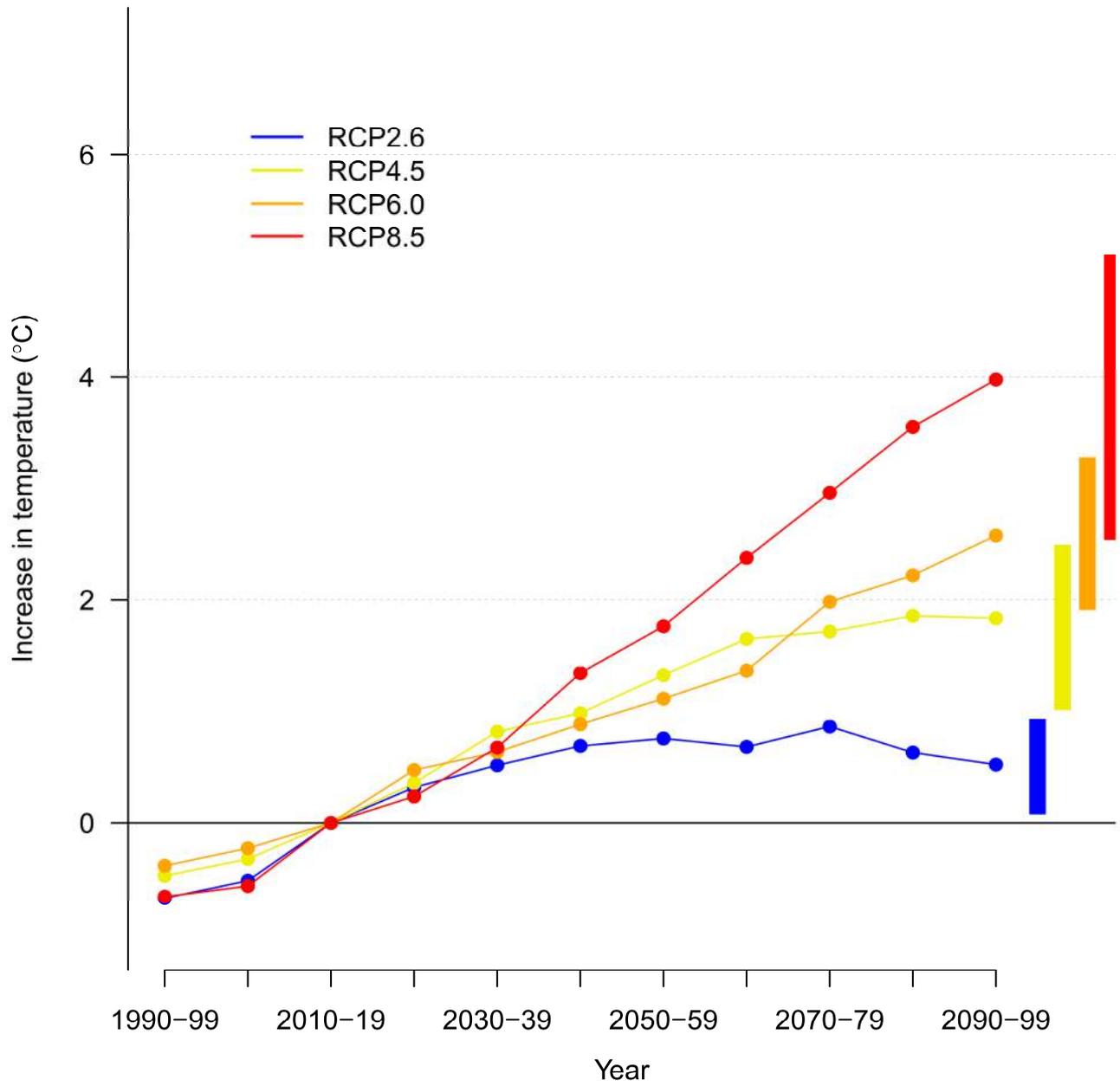


Figure 2

Japan (47 prefectures)

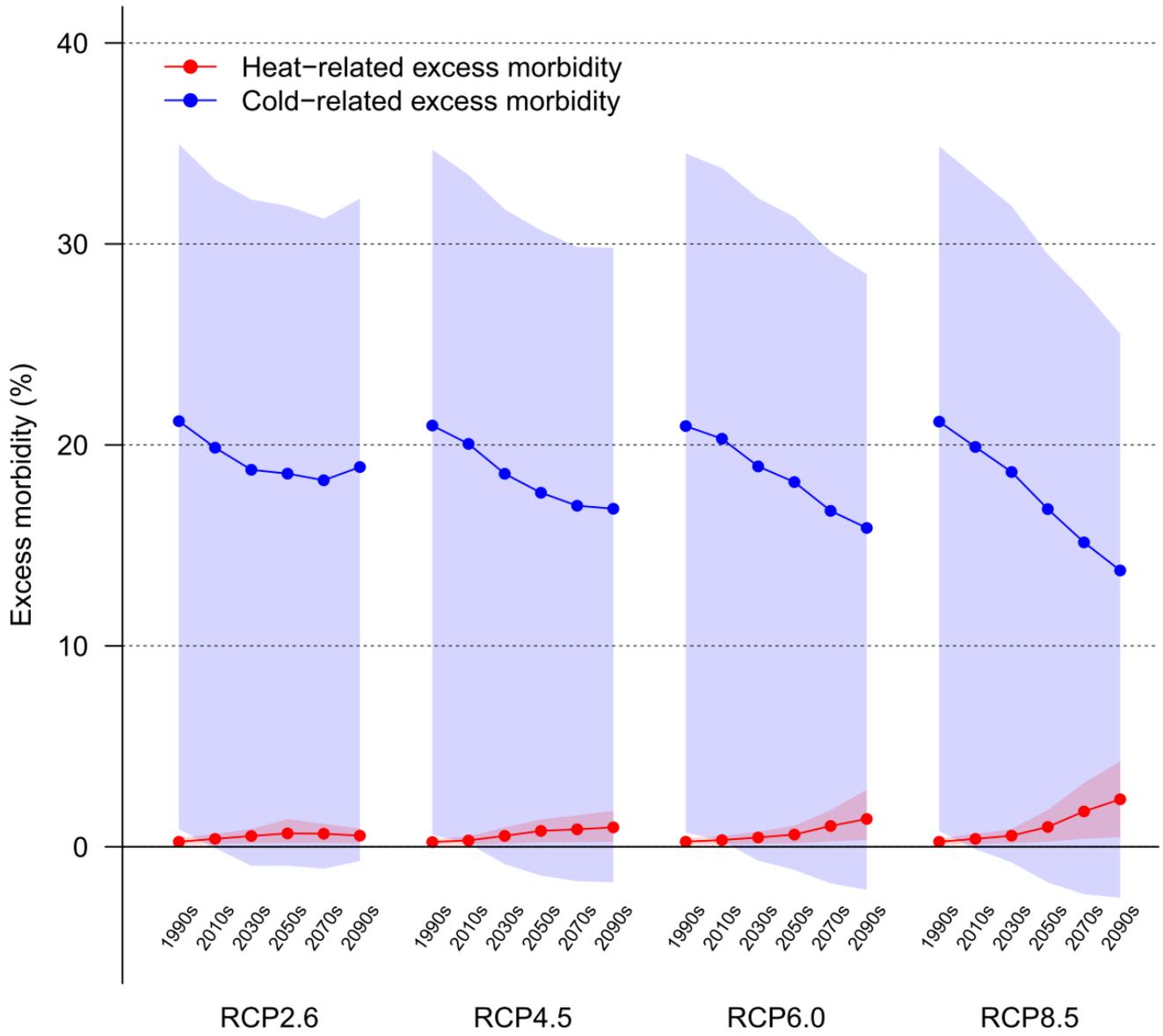


Figure 3

Japan (47 prefectures)

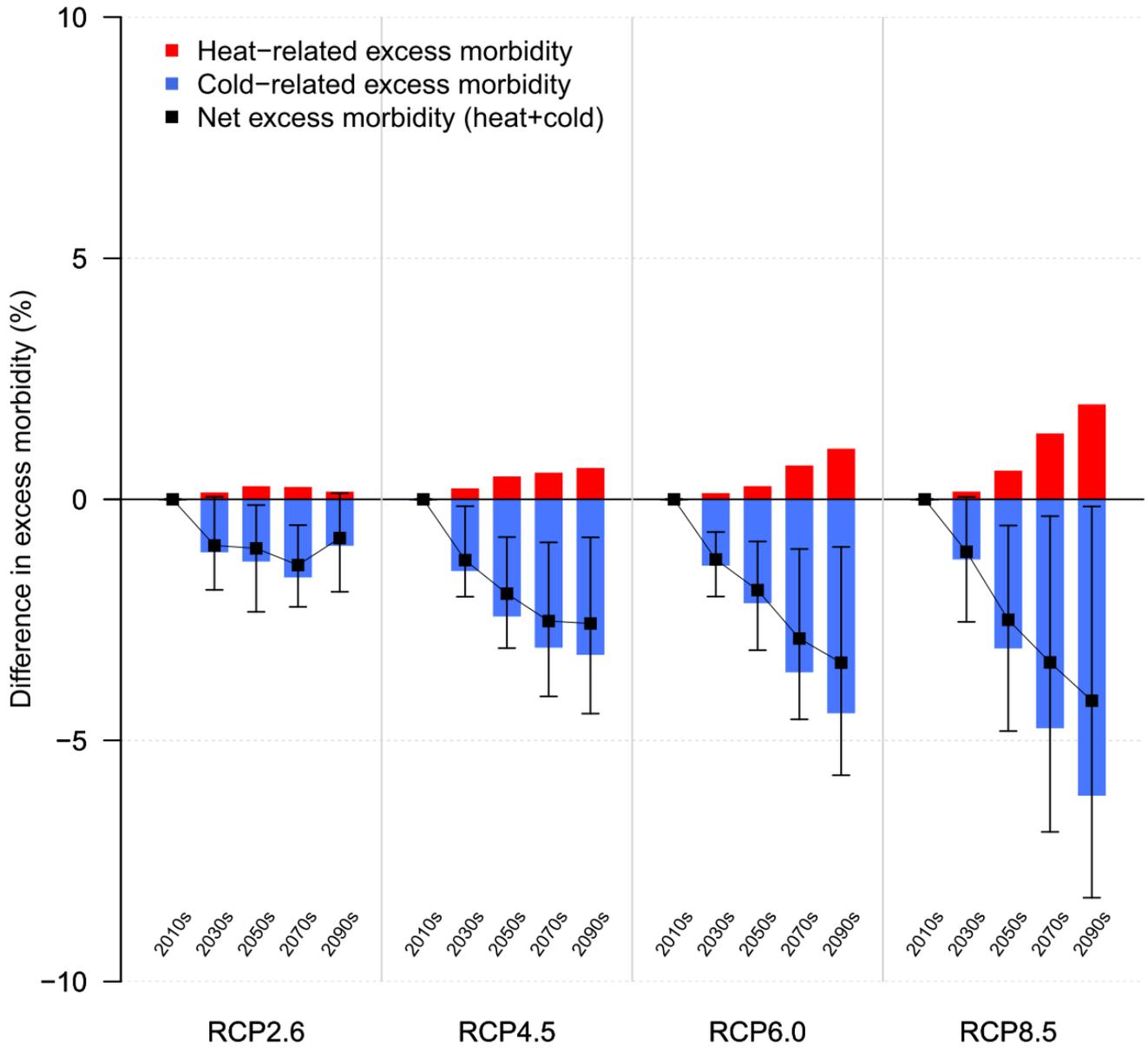


Figure 4