

Deutsches Ärzteblatt

Heat-related myocardial infarctions under and beyond Paris Agreement goals in Augsburg, Germany --Manuskript-Entwurf--

Manuskriptnummer:	DAEB-2019-048R1
Vollständiger Titel:	Heat-related myocardial infarctions under and beyond Paris Agreement goals in Augsburg, Germany
Artikeltyp:	Originalarbeit (max.2300 Wörter)
Korrespond. Autor:	Kai Chen, Ph.D. Helmholtz Zentrum Munchen Deutsches Forschungszentrum für Umwelt und Gesundheit Neuherberg, München GERMANY
Korrespondierender Autor, Zweitinformationen:	
Korrespondierender Autor, Institution:	Helmholtz Zentrum Munchen Deutsches Forschungszentrum für Umwelt und Gesundheit
Korrespondierender Autor, zweite Institution:	
Erstautor:	Kai Chen, Ph.D.
Erstautor, Zweitinformationen:	
Reihenfolge der Autoren:	Kai Chen, Ph.D. Susanne Breitner, Dr. rer. nat. Kathrin Wolf, Dr. rer. biol. hum. Masna Rai, BSc Christa Meisinger, Prof. Dr. med. Margit Heier, Dr. med. Bernhard Kuch, Prof. Dr. med. Annette Peters, Prof. Dr. rer. biol. hum. Alexandra Schneider, Dr. rer. biol. hum.
Reihenfolge 'Zweite Informationen' von Autoren:	
Zusammenfassung:	<p>Summary</p> <p>Background: Substantial efforts will be undertaken to limit global warming to 1.5 °C or 2 °C (Paris Agreement goals). Here, we aimed to project future heat-related myocardial infarction (MI) events in Augsburg, Germany, at increases in warming of 1.5 °C, 2 °C and 3 °C.</p> <p>Methods: Using daily time-series of MI cases and temperature projections under three climate scenarios, we projected changes in heat-related MIs at different increases in warming, assuming no future changes in population and adaptation.</p> <p>Results: Under a low emission scenario that limits warming below 2 °C throughout the 21st century, heat-related MI cases will increase by 17 (-1 to 46) per decade at 1.5 °C of warming. Under a high emission scenario, heat-related MI cases will increase by 32 (1 to 83), 54 (1 to 124), and 109 (4 to 313) per decade in warming of 1.5 °C, 2 °C and 3 °C, respectively. Similar results were found under a moderate emission scenario that fails to hold warming below 2 °C.</p> <p>Conclusion: The future burden of heat-related MIs in Augsburg will rise with any increase in warming. Fulfilling the Paris Agreement goals will lead to substantial health</p>

benefits for MI patients.

Zusammenfassung

Hintergrund: Es werden erhebliche Anstrengungen unternommen, um die globale Erwärmung auf 1,5 ° C oder 2 ° C zu begrenzen (Ziele des Pariser Übereinkommens). Unsere Zielsetzung war, zukünftige hitzebedingte Herzinfarktereignisse (HI) in Augsburg in Bezug auf eine globale Erwärmung um 1,5 ° C, 2 ° C bzw. 3 ° C zu projizieren.

Methoden: Unter Verwendung von täglichen HI-Zeitreihen und Temperaturprojektionen wurden basierend auf drei Klimaszenarien jeweils die Änderungen der hitzebedingten HIs in Bezug auf unterschiedliche Erwärmungslevel projiziert. Dabei wurden mögliche Änderungen der Bevölkerungsstruktur oder eine potentielle Adaptation der Bevölkerung nicht berücksichtigt.

Ergebnisse: In einem emissionsarmen Szenario, das die Erwärmung im gesamten 21. Jahrhundert auf unter 2 ° C begrenzt, werden hitzebedingte HIs bei 1,5 ° C globaler Erwärmung um 17 Fälle (-1 bis 46) pro Jahrzehnt zunehmen. In einem Szenario mit hohen Emissionen steigen die hitzebedingten HI-Fälle bei Erwärmung um 1,5 ° C, 2 ° C bzw. 3 ° C pro Jahrzehnt um 32 (1 bis 83), 54 (1 bis 124) bzw. 109 (4 bis 313) an. Ähnliche Ergebnisse wurden unter einem gemäßigten Emissionsszenario gefunden, bei dem die Erwärmung nicht unter 2 ° C gehalten werden kann.

Fazit: Mit zunehmender globaler Erwärmung steigt die künftige Belastung durch hitzebedingte HI-Fälle in Augsburg. Die Erfüllung der Ziele des Pariser Übereinkommens wird daher zu erheblichen gesundheitlichen Vorteilen für HI-Patienten führen.

1 **Heat-related myocardial infarctions under and beyond Paris Agreement**
2 **goals in Augsburg, Germany**

3 Kai Chen*, Susanne Breitner, Kathrin Wolf, Masna Rai, Christa Meisinger, Margit Heier,
4 Bernhard Kuch, Annette Peters, and Alexandra Schneider, for the KORA Study Group

5
6 **Affiliation:**

7 Institute of Epidemiology, Helmholtz Zentrum München–German Research Center for
8 Environmental Health: Dr. Chen, Dr. rer. nat. Breitner, Dr. rer. biol. hum. Wolf, Rai BSc, Dr.
9 med. Heier, Prof. Dr. rer. biol. hum. Peters, and Dr. rer. biol. hum. Schneider

10 Institute for Medical Information Processing, Biometry and Epidemiology, Ludwig-
11 Maximilians-Universität München: Dr. rer. nat. Breitner and Prof. Dr. rer. biol. hum. Peters
12 Ludwig-Maximilians-Universität München, Chair of Epidemiology at UNIKA-T: Prof. Dr.
13 med. Meisinger

14 Independent Research Group Clinical Epidemiology, Helmholtz Zentrum München–German
15 Research Center for Environmental Health: Prof. Dr. med. Meisinger

16 MONICA/KORA Myocardial Infarction Registry, University Hospital of Augsburg: Prof. Dr.
17 med. Meisinger

18 KORA Study Centre, University Hospital of Augsburg: Dr. med. Heier

19 Department of Internal Medicine I - Cardiology, University Hospital of Augsburg: Prof. Dr.
20 med. Kuch

21 Department of Internal Medicine/Cardiology, Hospital of Nördlingen: Prof. Dr. med. Kuch

22 German Research Center for Cardiovascular Research (DZHK), Partner-Site Munich: Prof.
23 Dr. rer. biol. hum. Peters

24
25 The KORA-Study Group consists of A. Peters (speaker), H. Schulz, L. Schwettmann, R.
26 Leidl, M. Heier, K. Strauch, and their co-workers, who are responsible for the design and
27 conduct of the KORA studies.

28
29 *** Corresponding author.** Tel: +49 89 3187-3697, Fax: +49 89 3187-3380, Email:

30 kai.chen@helmholtz-muenchen.de; kai.chen@yale.edu

31

32 **Number of words in the main text:** 2299 (excluding summary, references, legends, and
33 acknowledgement)

34 **Number of words in the summary:** 195

35 **Number of references:** 28

36 **Number of figures and tables:** 4

37 **Summary**

38 **Background:** Substantial efforts will be undertaken to limit global warming to 1.5 °C or 2 °C
39 (Paris Agreement goals). Here, we aimed to project future heat-related myocardial infarction
40 (MI) events in Augsburg, Germany, at increases in warming of 1.5 °C, 2 °C and 3 °C.

41 **Methods:** Using daily time-series of MI cases and temperature projections under three
42 climate scenarios, we projected changes in heat-related MIs at different increases in warming,
43 assuming no future changes in population and adaptation.

44 **Results:** Under a low emission scenario that limits warming below 2 °C throughout the 21st
45 century, heat-related MI cases will increase by 17 (-1 to 46) per decade at 1.5 °C of warming.
46 Under a high emission scenario, heat-related MI cases will increase by 32 (1 to 83), 54 (1 to
47 124), and 109 (4 to 313) per decade in warming of 1.5 °C, 2 °C and 3 °C, respectively.
48 Similar results were found under a moderate emission scenario that fails to hold warming
49 below 2 °C.

50 **Conclusion:** The future burden of heat-related MIs in Augsburg will rise with any increase in
51 warming. Fulfilling the Paris Agreement goals will lead to substantial health benefits for MI
52 patients.

53

54 **Keywords:** Climate change, Paris Agreement, Heat, Myocardial infarction, Projection

55

56 **Zusammenfassung**

57 **Hintergrund:** Es werden erhebliche Anstrengungen unternommen, um die globale
58 Erwärmung auf 1,5 ° C oder 2 ° C zu begrenzen (Ziele des Pariser Übereinkommens). Unsere
59 Zielsetzung war, zukünftige hitzebedingte Herzinfarktereignisse (HI) in Augsburg in Bezug
60 auf eine globale Erwärmung um 1,5 ° C, 2 ° C bzw. 3 ° C zu projizieren.

61 **Methoden:** Unter Verwendung von täglichen HI-Zeitreihen und Temperaturprojektionen
62 wurden basierend auf drei Klimaszenarien jeweils die Änderungen der hitzebedingten HIs in
63 Bezug auf unterschiedliche Erwärmungslevel projiziert. Dabei wurden mögliche Änderungen
64 der Bevölkerungsstruktur oder eine potentielle Adaptation der Bevölkerung nicht
65 berücksichtigt.

66 **Ergebnisse:** In einem emissionsarmen Szenario, das die Erwärmung im gesamten 21.
67 Jahrhundert auf unter 2 ° C begrenzt, werden hitzebedingte HIs bei 1,5 ° C globaler
68 Erwärmung um 17 Fälle (-1 bis 46) pro Jahrzehnt zunehmen. In einem Szenario mit hohen
69 Emissionen steigen die hitzebedingten HI-Fälle bei Erwärmung um 1,5 ° C, 2 ° C bzw. 3 ° C
70 pro Jahrzehnt um 32 (1 bis 83), 54 (1 bis 124) bzw. 109 (4 bis 313) an. Ähnliche Ergebnisse
71 wurden unter einem gemäßigten Emissionsszenario gefunden, bei dem die Erwärmung nicht
72 unter 2 ° C gehalten werden kann.

73 **Fazit:** Mit zunehmender globaler Erwärmung steigt die künftige Belastung durch
74 hitzebedingte HI-Fälle in Augsburg. Die Erfüllung der Ziele des Pariser Übereinkommens
75 wird daher zu erheblichen gesundheitlichen Vorteilen für HI-Patienten führen.

76

77 **Introduction**

78 Climate change is the biggest global health threat and tackling it could be the greatest global
79 health opportunity of the 21st century (1). To reduce the health risks of climate change, the
80 United Nations Framework Convention on Climate Change (UNFCCC) adopted the Paris
81 Agreement in 2015, which aims at holding global warming to well below 2 °C above pre-
82 industrial levels and pursuing efforts to limit it to 1.5 °C (2). However, little is known about
83 the difference in health impacts between the 1.5 °C and 2 °C warming targets (3, 4). Although
84 emerging evidence from regional, national, and global studies show a potential increase in
85 temperature-related mortality under climate change (5-9), nearly all these studies focused on a
86 certain future period but not on a specific warming target (3). Thus, it remains unclear
87 whether limiting global warming to 1.5 °C instead of 2 °C will avoid temperature-related
88 health impacts (3, 10).

89 In October 2018, the Intergovernmental Panel on Climate Change (IPCC) provided a Special
90 Report on the impacts of global warming of 1.5 °C (SR15) and concluded with a very high
91 confidence that heat-related health impact will be greater at 2 °C than at 1.5 °C of global
92 warming (11). However, most of the previous projection studies have been focusing on
93 mortality rather than morbidity (12), leading to limited evidence of climate change impacts on
94 heat-related morbidity. Our recent study found that heat exposure is a potential trigger of MI
95 events (13). Plausible pathophysiological mechanism is shown in *Box 1*. Here, we aimed to
96 project future heat-related myocardial infarction (MI) events in Augsburg, Germany, at
97 warming of degrees consistent with the Paris Agreement goals (1.5 °C and 2 °C) and higher
98 (3 °C). This information can help the health professionals and policy makers to better
99 understand the potential health threat of climate change.

100 **Methods**

101 **Study population**

102 We collected data from the population-based Cooperative Health Research in the Region of
103 Augsburg (KORA) MI registry. The study area includes the city of Augsburg and the two
104 adjacent counties (Augsburg and Aichach-Friedberg). We used all recorded cases of MI and
105 coronary deaths among residents aged 25 to 74 (about 400,000 inhabitants) from January 1,
106 2001, to December 31, 2014. We further analyzed subtypes of MI events including ST-
107 segment elevation MI (STEMI) and non-ST segment elevation MI (NSTEMI) events. Details
108 of this registry are given in the *eMethods*. This study was approved by the ethics committee of

109 Bavarian Chamber of Physicians and performed in accordance with the Declaration of
110 Helsinki.

111 **Temperature projections**

112 We obtained daily mean temperatures during 2010-2099 from four global climate models
113 under the Inter-Sectoral Impact Model Intercomparison Project Phase 2b (ISIMIP2b) (14). We
114 used three climate change scenarios under the Representative Concentration Pathway (RCP)
115 2.6, RCP4.5, and RCP8.5, corresponding to low, moderate, and high warming and emission
116 scenarios, respectively (*Box 2*). We applied the method described in Ebi et al. (2018) (3) to
117 determine the period when 1.5 °C, 2 °C, and 3 °C of warming above pre-industrial levels will
118 be reached, using the decade 2010-2019 as a baseline (*eMethods*).

119 **Health impact assessment**

120 We estimated the number and fraction of MI cases attributable to heat exposure under
121 different degrees of warming based on the assumption of no future changes in population and
122 adaptation, using a recently developed approach (15). Briefly, we applied the previously
123 estimated exposure-response functions between daily mean temperature and daily MI events
124 (*eFigure 1*) (13), the temperature projections, and baseline MI cases to calculate the daily
125 attributable number of MI events. The baseline MI cases were calculated as the average
126 observed number of cases for each day of the year during 2001-2014. Finally, we computed
127 the future changes as the differences between the future decades reaching different degrees of
128 warming and the baseline period for each RCP. We used Monte Carlo simulations to estimate
129 empirical confidence interval (eCI) to address the uncertainty in exposure-response functions
130 and the variability across global climate models. Key elements in the assessment are provided
131 in *eBox*. Details of the health impact assessment can be found in the *eMethods*.

132 **Results**

133 *Figure 1* shows the 10-year moving average global-mean-temperature projections from the
134 average of four global climate models under three RCP scenarios relative to pre-industrial
135 levels. Global-mean-temperature under RCP4.5 and RCP8.5 exceeds 3 °C relative to pre-
136 industrial levels by the end of the 21st century, whereas it remains below 2 °C under RCP2.6.
137 In general, warming of 1.5 °C and 2 °C will be reached around 2030 and 2040, respectively
138 (*Table 1*). Warming of 3 °C will be reached around 2070 under RCP4.5, whereas under
139 RCP8.5 it will be reached 20 years earlier.

140 Over 2001-2014, there were on average 967 coronary events per year, among which 235 were
141 STEMI and 331 were NSTEMI. Relative to the baseline period, heat-related MIs will increase
142 under all warming scenarios and all RCPs (*Table 2*). When meeting the Paris Agreement
143 target of limiting warming to 1.5 °C, heat-related MI cases per decade in Augsburg will
144 increase by 17 (95% eCI: -1 to 46), 28 (0 to 94), and 32 (1 to 83) under RCP2.6, RCP4.5, and
145 RCP8.5, respectively. Compared to 1.5 °C of warming, 2 °C of warming generally yields
146 larger increases in heat-related MIs, with a significant increase of 51 (3 to 108) for RCP4.5
147 and 54 (1 to 124) for RCP8.5. When beyond the Paris Agreement target at 3 °C of warming,
148 heat-related MIs are projected to increase by 106 (3 to 287) for RCP4.5 and 109 (4 to 313) for
149 RCP8.5, which correspond to about 1.1% increase in the heat-attributable burden of MI cases.
150 *Figure 2* summarizes the changes in heat-related MIs under different warming scenarios for
151 total and subtypes of MI. With regard to the change of attributable cases, total, STEMI, and
152 NSTEMI events are generally projected to increase with increasing warming degrees. Most of
153 the increased heat-related MIs are NSTEMI events, with the increase ranging from 12 (2 to
154 27) in 1.5 °C of warming under RCP2.6 to 70 (11 to 171) in 3 °C of warming.

155 **Discussion**

156 Our analyses show that any increase in global warming is projected to increase heat-related
157 MIs in Augsburg, Germany. Holding warming at 1.5 °C instead of 2 °C or 3 °C will avoid a
158 substantial number of heat-related MIs. Under RCP2.6, warming will be limited below 2 °C
159 by 2100 and result in a smaller increase of heat-related MIs. On the contrary, warming by
160 2100 will be higher than 3 °C under RCP4.5 and RCP8.5, leading to a considerable increasing
161 burden of MIs.

162 Very few studies have directly estimated the regional health impacts of stabilizing climate
163 warming at 1.5 °C instead of 2 °C (3). Our finding of increasing heat-related impacts for
164 warming at 2 °C than at 1.5 °C is consistent with the conclusion of the IPCC SR15 report (11)
165 and the findings of two recent studies covering European cities (10, 16). We also found a
166 large reduction in heat-related total MIs in Augsburg between 2 °C and 3 °C under both the
167 moderate emission scenario RCP4.5 and the high emission scenario RCP8.5. This suggests
168 that the emission reduction trajectories towards the Paris Agreement goals can avoid heat-
169 related impacts on MI burden.

170 Among the climate scenarios, RCP2.6 meets the Paris Agreement target of keeping warming
171 well below 2 °C (*Figure 1 and Table 1*), which is in line with a previous review (3). When
172 limiting warming to 1.5 °C under RCP2.6, heat-related MIs are projected to account for 0.2%

173 (0% to 0.5%) of total MI burden. In comparison, heat-related MIs under RCP4.5 and RCP8.5
174 will be 2 times larger (0.5%-0.6%) under 2 °C of warming and 5 times larger (1.1%) under
175 3 °C of warming (*Table 2*). Similarly, a previous study also estimated a much smaller increase
176 in heat-related mortality over the 21st century under RCP2.6 compared to RCP4.5 and RCP8.5
177 in central and southern European cities (5).

178 According to the Federal Statistical Office, 135,218 MI events occurred in patients aged
179 between 25 and 74 in Germany in 2015 (including both acute MI patients and cardiac arrest
180 deaths) (17). If our projected changes in attributable fractions in the Augsburg region could be
181 applied to the whole of Germany, a back-of-envelope calculation shows that holding warming
182 at 1.5 °C under RCP2.6 relative to a 3 °C of warming following the high emission pathway
183 RCP8.5 would prevent 1,217 MI cases each year. This number is likely to be underestimated
184 as we only considered patients aged below 75 whereas the elderly have been demonstrated to
185 be more vulnerable to heat-related mortality and morbidity (18, 19). Our findings suggest that
186 ambitious greenhouse gas emission reductions are required to achieve the Paris Agreement
187 targets and to prevent adverse temperature-related health impacts.

188 **Implications for healthcare professionals**

189 Healthcare professionals have vital roles in accelerating progress to tackle climate change, as
190 they are trained to educate patients about health threats, may be trusted more than
191 environmentalists, and can better communicate the health risks posed by climate change and
192 inform public policy to reduce greenhouse gases emissions (1, 20). With the ability to
193 effectively advocate against the health threats of climate change, healthcare professionals
194 should take a lead in fighting climate change (21). To encourage general practitioners and
195 other health professionals to lead on tackling climate change, it is important to understand
196 how climate change can impact health outcomes (22). This study suggests that any additional
197 degrees of warming can result in increasing heat-related MI cases, calling on healthcare
198 professionals to inform public and policymakers about potential health threats of climate
199 change and benefits of taking climate actions to protect health.

200 **Strengths and limitations**

201 To the best of our knowledge, this is the first study projecting heat-related MIs under and
202 beyond Paris Agreement goals. Our estimates are based on a validated, complete, and detailed
203 registration of all MI and coronary death cases in Augsburg, in combination with an advanced
204 and established approach to account for uncertainty in exposure-response functions and
205 variability across climate models (5). Our estimates could be interpreted as the changes in

206 heat-related MIs if the current Augsburg population were exposed to future temperatures
207 under global warming of 1.5 °C, 2 °C and 3 °C. Thus, our projections allow isolation of the
208 effects of a changing climate from other factors such as demographic change and population
209 adaptation (5).

210 Our study has several limitations. First, our projections of the health impacts focus on specific
211 Paris Agreement targets rather than consistent future periods. This approach used different
212 periods for different warming targets (e.g., 2022-2031 for 1.5 °C and 2032-2041 for 2 °C
213 under RCP8.5), which limits our ability to consider impacts of future population changes in
214 size, age structure, lifestyle, and underlying MI rates. As we expect more NSTEMI events but
215 less STEMI events occurring in the future in Augsburg (13), the future changes in total
216 temperature-related MI burden may be underestimated. Moreover, the temperature projections
217 we used have a relatively coarse spatial resolution (~ 50 km). Future studies using higher
218 resolution temperature projections, such as the temperature projections from COSMO-CLM
219 developed by Deutscher Wetterdienst, are warranted to estimate regional health impact of
220 climate change. Furthermore, we did not consider population adaptation to heat (23).
221 However, heat-related vulnerability may further increase in Augsburg (13), resulting in an
222 increased future temperature-related impacts.

223 **Conclusion**

224 The burden of heat-related MIs in Augsburg will increase with any degree increase in global
225 warming, with a smaller burden at 1.5 °C than at 2 °C or 3 °C. Compared with a high
226 emission scenario, limiting global warming at 1.5 °C under a low emission scenario will lead
227 to substantial health benefits for MI patients, suggesting that climate change mitigation
228 policies are needed to fulfill the Paris Agreement goals.

229

230 **Key messages**

- 231 • Any increase in global warming will increase heat-related MIs.
- 232 • Compared to 2 °C of warming, 1.5 °C of warming reduces about half of all heat-
233 related MIs.
- 234 • Under a high emission pathway, heat-related MIs at 3 °C will be 5 times larger than at
235 1.5 °C under a low emission pathway.
- 236 • Failing to meet the Paris Agreement goal will result in a substantial increase in heat-
237 related MIs, especially for NSTEMI events.

238 **Box 1. Potential pathophysiological link between heat exposure and myocardial**
239 **infarction**

240 Heat exposure may lead to the onset of myocardial infarction through 1) vasodilation and
241 increased surface blood circulation, which may increase cardiac work load and result in
242 hemoconcentration and thrombosis promotion, and 2) releasing interleukins that modulate
243 local and systemic inflammation and result in endothelial dysfunction (24, 25). Potential
244 mechanisms for the heat exposure effects on myocardial infarction are shown in Figure Box1.

245

246 **Box 2. Climate change scenarios**

247 The Intergovernmental Panel on Climate Change (IPCC) uses Representative Concentration
248 Pathways (RCPs) to describe different 21st century trajectories of greenhouse gases emissions
249 and atmospheric concentrations, air pollution emissions, and land use (26). The numbers in
250 RCPs correspond to different target levels of radiative forcing in 2100. Radiative forcing
251 reflects the effect of greenhouse gases and aerosols on the Earth's energy balance. Three
252 RCPs were used in this study, including a stringent emission mitigation scenario (RCP2.6),
253 one intermediate scenario (RCP4.5), and one scenario with very high greenhouse gases
254 emissions (RCP8.5).

- 255 • RCP2.6 aims to limit global warming below 2 °C and requires substantial net negative
256 emissions by 2100, with an average of about 2 Gt/year for CO₂ emissions (27).
- 257 • RCP4.5 is a scenario that stabilizes radiative forcing by 2100, with CO₂ emissions
258 peak around 42 Gt/year in 2040 and decline to 2080 before leveling off around 15
259 Gt/year (28).
- 260 • RCP8.5 assumes no additional mitigation efforts to reduce emissions (or the so-called
261 “Business-as-usual” scenario), with an average CO₂ emissions of 73 Gt/year over the
262 21st century (29).

263 Relative to 1986-2005, global mean sea level rise in 2081-2100 will likely be 0.40 m, 0.47 m,
264 and 0.63 m under RCP2.6, RCP4.5, and RCP8.5, respectively.

265

266 **Funding**

267 KC acknowledges support from the Alexander von Humboldt Foundation for the Humboldt
268 Research Fellowship. The KORA research platform was initiated and financed by the
269 Helmholtz Zentrum München, German Research Center for Environmental Health, which is
270 funded by the German Federal Ministry of Education, Science, Research, and Technology and
271 by the State of Bavaria. Since 2000, the MI data collection has been co-financed by the
272 German Federal Ministry of Health and Social Security to provide population-based MI
273 morbidity data for the official German Health Report (see www.gbe-bund.de).

274 **Conflict of interest statement**

275 None.

276

277 **References**

- 278 1. Watts N, Adger WN, Agnolucci P, et al.: Health and climate change: policy responses to
279 protect public health. *Lancet* 2015; 386: 1861-914.
- 280 2. UNFCCC: Adoption of the Paris agreement. Report No FCCC/CP/2015/L9/Rev12015.
- 281 3. Ebi KL, Hasegawa T, Hayes K, Monaghan A, Paz S, Berry P: Health risks of warming of 1.5°
282 C, 2° C, and higher, above pre-industrial temperatures. *Environ Res Lett* 2018; 13: 063007.
- 283 4. Shindell D, Faluvegi G, Seltzer K, Shindell C: Quantified, localized health benefits of
284 accelerated carbon dioxide emissions reductions. *Nat Clim Chang* 2018; 8: 291-5.
- 285 5. Gasparrini A, Guo Y, Sera F, et al.: Projections of temperature-related excess mortality under
286 climate change scenarios. *Lancet Planet Health* 2017; 1: e360-e7.
- 287 6. Weinberger KR, Haykin L, Eliot MN, Schwartz JD, Gasparrini A, Wellenius GA: Projected
288 temperature-related deaths in ten large U.S. metropolitan areas under different climate change
289 scenarios. *Environ Int* 2017; 107: 196-204.
- 290 7. Chen K, Horton RM, Bader DA, et al.: Impact of climate change on heat-related mortality in
291 Jiangsu Province, China. *Environ Pollut* 2017; 224: 317-25.
- 292 8. Guo Y, Gasparrini A, Li S, et al.: Quantifying excess deaths related to heatwaves under
293 climate change scenarios: A multicountry time series modelling study. *PLoS Med* 2018; 15: e1002629.
- 294 9. Li T, Horton RM, Kinney PL: Projections of seasonal patterns in temperature-related deaths
295 for Manhattan, New York. *Nat Clim Chang* 2013; 3: 717.
- 296 10. Mitchell D, Heaviside C, Schaller N, et al.: Extreme heat-related mortality avoided under Paris
297 Agreement goals. *Nat Clim Chang* 2018; 8: 551-3.
- 298 11. Hoegh-Guldberg O, Jacob D, Taylor M, et al.: Impacts of 1.5°C Global Warming on Natural
299 and Human Systems. In: Masson-Delmotte V, Zhai P, Pörtner H-O, et al., (eds.): *Global warming of
300 15°C An IPCC Special Report on the impacts of global warming of 15°C above pre-industrial levels
301 and related global greenhouse gas emission pathways, in the context of strengthening the global
302 response to the threat of climate change, sustainable development, and efforts to eradicate poverty: In
303 Press* 2018.
- 304 12. Weinberger KR, Kirwa K, Eliot MN, Gold J, Suh HH, Wellenius GA: Projected changes in
305 temperature-related morbidity and mortality in Southern New England. *Epidemiology* 2018; 29: 473-
306 81.
- 307 13. Chen K, Breitner S, Wolf K, et al.: Temporal variations in the triggering of myocardial
308 infarction by air temperature in Augsburg, Germany, 1987-2014. *Eur Heart J* 2019.

- 309 14. Frieler K, Lange S, Piontek F, et al.: Assessing the impacts of 1.5 °C global warming –
310 simulation protocol of the Inter-Sectoral Impact Model Intercomparison Project (ISIMIP2b). *Geosci*
311 *Model Dev* 2017; 10: 4321-45.
- 312 15. Gasparrini A, Leone M: Attributable risk from distributed lag models. *BMC Med Res*
313 *Methodol* 2014; 14: 55.
- 314 16. Vicedo-Cabrera AM, Guo Y, Sera F, et al.: Temperature-related mortality impacts under and
315 beyond Paris Agreement climate change scenarios. *Clim Change* 2018; 150: 391-402.
- 316 17. German Federal Statistical Office: Diagnoses of hospital patients [https://www-](https://www-genesis.destatis.de/genesis/online/data)
317 [genesis.destatis.de/genesis/online/data](https://www-genesis.destatis.de/genesis/online/data) (last accessed on January 7 2019).
- 318 18. Basu R: High ambient temperature and mortality: a review of epidemiologic studies from 2001
319 to 2008. *Environ Health* 2009; 8: 40.
- 320 19. Bell ML, O’Neill MS, Ranjit N, Borja-Aburto VH, Cifuentes LA, Gouveia NC: Vulnerability
321 to heat-related mortality in Latin America: a case-crossover study in São Paulo, Brazil, Santiago, Chile
322 and Mexico City, Mexico. *Int J Epidemiol* 2008; 37: 796-804.
- 323 20. McCoy D, Hoskins B: The science of anthropogenic climate change: what every doctor should
324 know. *BMJ* 2014; 349: g5178.
- 325 21. Ramanathan V, Haines A: Healthcare professionals must lead on climate change. *BMJ* 2016;
326 355: i5245.
- 327 22. Patz JA, Frumkin H, Holloway T, Vimont DJ, Haines A: Climate change: Challenges and
328 opportunities for global health. *JAMA* 2014; 312: 1565-80.
- 329 23. Petkova EP, Vink JK, Horton RM, et al.: Towards more comprehensive projections of urban
330 heat-related mortality: Estimates for New York City under multiple population, adaptation, and
331 climate scenarios. *Environ Health Perspect* 2017; 125: 47-55.
- 332 24. Schneider A, Ruckerl R, Breitner S, Wolf K, Peters A: Thermal control, weather, and aging.
333 *Curr Environ Health Rep* 2017; 4: 21-9.
- 334 25. Liu L, Breitner S, Pan X, et al.: Associations between air temperature and cardio-respiratory
335 mortality in the urban area of Beijing, China: a time-series analysis. *Environ Health* 2011; 10: 51.
- 336 26. IPCC: Climate Change 2014: Synthesis Report. Contribution of Working Groups I, II and III
337 to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change. Geneva,
338 Switzerland: IPCC; 2014.
- 339 27. van Vuuren DP, Stehfest E, den Elzen MGJ, et al.: RCP2.6: exploring the possibility to keep
340 global mean temperature increase below 2°C. *Clim Change* 2011; 109: 95-116.
- 341 28. Thomson AM, Calvin KV, Smith SJ, et al.: RCP4.5: a pathway for stabilization of radiative
342 forcing by 2100. *Clim Change* 2011; 109: 77-94.
- 343 29. Riahi K, Rao S, Krey V, et al.: RCP 8.5—A scenario of comparatively high greenhouse gas
344 emissions. *Clim Change* 2011; 109: 33-57.

345

346 **Figure Legends**

347 **Figure 1.** Time-series of 10-year moving average of annual global mean near-surface
348 temperature change relative to pre-industrial levels under different climate scenarios (RCPs).
349 X-axis denotes the start year of a 10-year moving window.

350

351 **Figure 2.** Changes in heat-related MI cases per decade projected for 1.5 °C, 2 °C, and 3 °C of
352 warming by MI types. Red and blue bars represent changes in the heat-related number of
353 STEMI and NSTEMI events in future warming decades relative to 2010-2019 under three
354 climate scenarios (RCP2.6, RCP4.5, and RCP8.5). Black dots and vertical lines denote
355 changes and 95% empirical CIs in the heat-related total number of MI events.

356

357 **Figure Box 1.** Plausible pathophysiological mechanisms linking heat exposure to myocardial
358 infarction.

359

360 **eFigure 1.** Overall lag-cumulative exposure-response functions between air temperature and
361 myocardial infarction with 95% confidence intervals in Augsburg, Germany during 2001-
362 2014. The exposure-response functions were obtained from Chen et al. (2019) (13). The red
363 lines represent heat effect (temperature above 18.4 °C), whereas blue lines represent cold
364 effect (temperature below 18.4 °C).

365

361 **Funding**

362 KC acknowledges support from the Alexander von Humboldt Foundation for the Humboldt
363 Research Fellowship. The KORA research platform was initiated and financed by the
364 Helmholtz Zentrum München, German Research Center for Environmental Health, which is
365 funded by the German Federal Ministry of Education, Science, Research, and Technology and
366 by the State of Bavaria. Since 2000, the MI data collection has been co-financed by the
367 German Federal Ministry of Health and Social Security to provide population-based MI
368 morbidity data for the official German Health Report (see www.gbe-bund.de).

369 **Conflict of interest statement**

370 None.

371

372 **References**

- 373 1. Watts N, Adger WN, Agnolucci P, et al.: Health and climate change: policy responses to
374 protect public health. *Lancet* 2015; 386: 1861-914.
- 375 2. UNFCCC: Adoption of the Paris agreement. Report No FCCC/CP/2015/L9/Rev12015.
- 376 3. Ebi KL, Hasegawa T, Hayes K, Monaghan A, Paz S, Berry P: Health risks of warming of 1.5°
377 C, 2° C, and higher, above pre-industrial temperatures. *Environ Res Lett* 2018; 13: 063007.
- 378 4. Shindell D, Faluvegi G, Seltzer K, Shindell C: Quantified, localized health benefits of
379 accelerated carbon dioxide emissions reductions. *Nat Clim Chang* 2018; 8: 291-5.
- 380 5. Gasparrini A, Guo Y, Sera F, et al.: Projections of temperature-related excess mortality under
381 climate change scenarios. *Lancet Planet Health* 2017; 1: e360-e7.
- 382 6. Weinberger KR, Haykin L, Eliot MN, Schwartz JD, Gasparrini A, Wellenius GA: Projected
383 temperature-related deaths in ten large U.S. metropolitan areas under different climate change
384 scenarios. *Environ Int* 2017; 107: 196-204.
- 385 7. Chen K, Horton RM, Bader DA, et al.: Impact of climate change on heat-related mortality in
386 Jiangsu Province, China. *Environ Pollut* 2017; 224: 317-25.
- 387 8. Guo Y, Gasparrini A, Li S, et al.: Quantifying excess deaths related to heatwaves under
388 climate change scenarios: A multicountry time series modelling study. *PLoS Med* 2018; 15: e1002629.
- 389 9. Li T, Horton RM, Kinney PL: Projections of seasonal patterns in temperature-related deaths
390 for Manhattan, New York. *Nat Clim Chang* 2013; 3: 717.
- 391 10. Mitchell D, Heaviside C, Schaller N, et al.: Extreme heat-related mortality avoided under Paris
392 Agreement goals. *Nat Clim Chang* 2018; 8: 551-3.
- 393 11. Hoegh-Guldberg O, Jacob D, Taylor M, et al.: Impacts of 1.5°C Global Warming on Natural
394 and Human Systems. In: Masson-Delmotte V, Zhai P, Pörtner H-O, et al., (eds.): *Global warming of
395 15°C An IPCC Special Report on the impacts of global warming of 15°C above pre-industrial levels
396 and related global greenhouse gas emission pathways, in the context of strengthening the global
397 response to the threat of climate change, sustainable development, and efforts to eradicate poverty: In
398 Press* 2018.
- 399 12. Weinberger KR, Kirwa K, Eliot MN, Gold J, Suh HH, Wellenius GA: Projected changes in
400 temperature-related morbidity and mortality in Southern New England. *Epidemiology* 2018; 29: 473-
401 81.
- 402 13. Chen K, Breitner S, Wolf K, et al.: Temporal variations in the triggering of myocardial
403 infarction by air temperature in Augsburg, Germany, 1987-2014. *Eur Heart J* 2019.

- 404 14. Frieler K, Lange S, Piontek F, et al.: Assessing the impacts of 1.5 °C global warming –
405 simulation protocol of the Inter-Sectoral Impact Model Intercomparison Project (ISIMIP2b). *Geosci*
406 *Model Dev* 2017; 10: 4321-45.
- 407 15. Gasparrini A, Leone M: Attributable risk from distributed lag models. *BMC Med Res*
408 *Methodol* 2014; 14: 55.
- 409 16. Vicedo-Cabrera AM, Guo Y, Sera F, et al.: Temperature-related mortality impacts under and
410 beyond Paris Agreement climate change scenarios. *Clim Change* 2018; 150: 391-402.
- 411 17. German Federal Statistical Office: Diagnoses of hospital patients [https://www-](https://www-genesis.destatis.de/genesis/online/data)
412 [genesis.destatis.de/genesis/online/data](https://www-genesis.destatis.de/genesis/online/data) (last accessed on January 7 2019).
- 413 18. Basu R: High ambient temperature and mortality: a review of epidemiologic studies from 2001
414 to 2008. *Environ Health* 2009; 8: 40.
- 415 19. Bell ML, O'Neill MS, Ranjit N, Borja-Aburto VH, Cifuentes LA, Gouveia NC: Vulnerability
416 to heat-related mortality in Latin America: a case-crossover study in São Paulo, Brazil, Santiago, Chile
417 and Mexico City, Mexico. *Int J Epidemiol* 2008; 37: 796-804.
- 418 20. McCoy D, Hoskins B: The science of anthropogenic climate change: what every doctor should
419 know. *BMJ* 2014; 349: g5178.
- 420 21. Ramanathan V, Haines A: Healthcare professionals must lead on climate change. *BMJ* 2016;
421 355: i5245.
- 422 22. Patz JA, Frumkin H, Holloway T, Vimont DJ, Haines A: Climate change: Challenges and
423 opportunities for global health. *JAMA* 2014; 312: 1565-80.
- 424 23. Petkova EP, Vink JK, Horton RM, et al.: Towards more comprehensive projections of urban
425 heat-related mortality: Estimates for New York City under multiple population, adaptation, and
426 climate scenarios. *Environ Health Perspect* 2017; 125: 47-55.
- 427 24. Schneider A, Ruckerl R, Breitner S, Wolf K, Peters A: Thermal control, weather, and aging.
428 *Curr Environ Health Rep* 2017; 4: 21-9.
- 429 25. Liu L, Breitner S, Pan X, et al.: Associations between air temperature and cardio-respiratory
430 mortality in the urban area of Beijing, China: a time-series analysis. *Environ Health* 2011; 10: 51.
- 431 26. IPCC: Climate Change 2014: Synthesis Report. Contribution of Working Groups I, II and III
432 to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change. Geneva,
433 Switzerland: IPCC; 2014.
- 434 27. van Vuuren DP, Stehfest E, den Elzen MGJ, et al.: RCP2.6: exploring the possibility to keep
435 global mean temperature increase below 2°C. *Clim Change* 2011; 109: 95-116.
- 436 28. Thomson AM, Calvin KV, Smith SJ, et al.: RCP4.5: a pathway for stabilization of radiative
437 forcing by 2100. *Clim Change* 2011; 109: 77-94.
- 438 29. Riahi K, Rao S, Krey V, et al.: RCP 8.5—A scenario of comparatively high greenhouse gas
439 emissions. *Clim Change* 2011; 109: 33-57.

440

Table 1. Decades when 1.5 °C, 2 °C, and 3 °C of global warming are projected to be reached.*

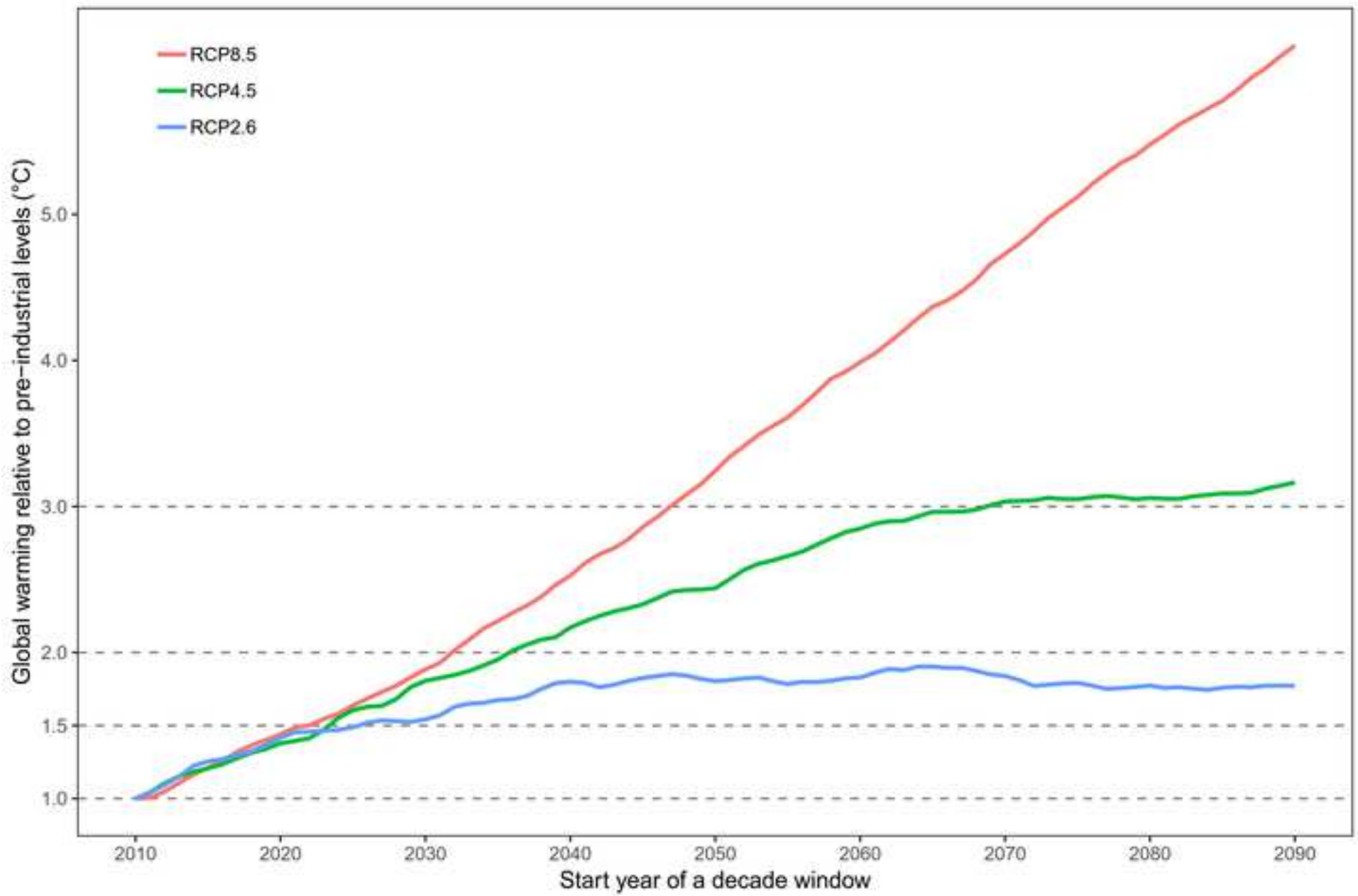
RCP	Decade 1.5 °C reached	Decade 2 °C reached	Decade 3 °C reached
RCP2.6	2026-2035	Not reached	Not reached
RCP4.5	2024-2033	2036-2045	2069-2078
RCP8.5	2022-2031	2032-2041	2047-2056

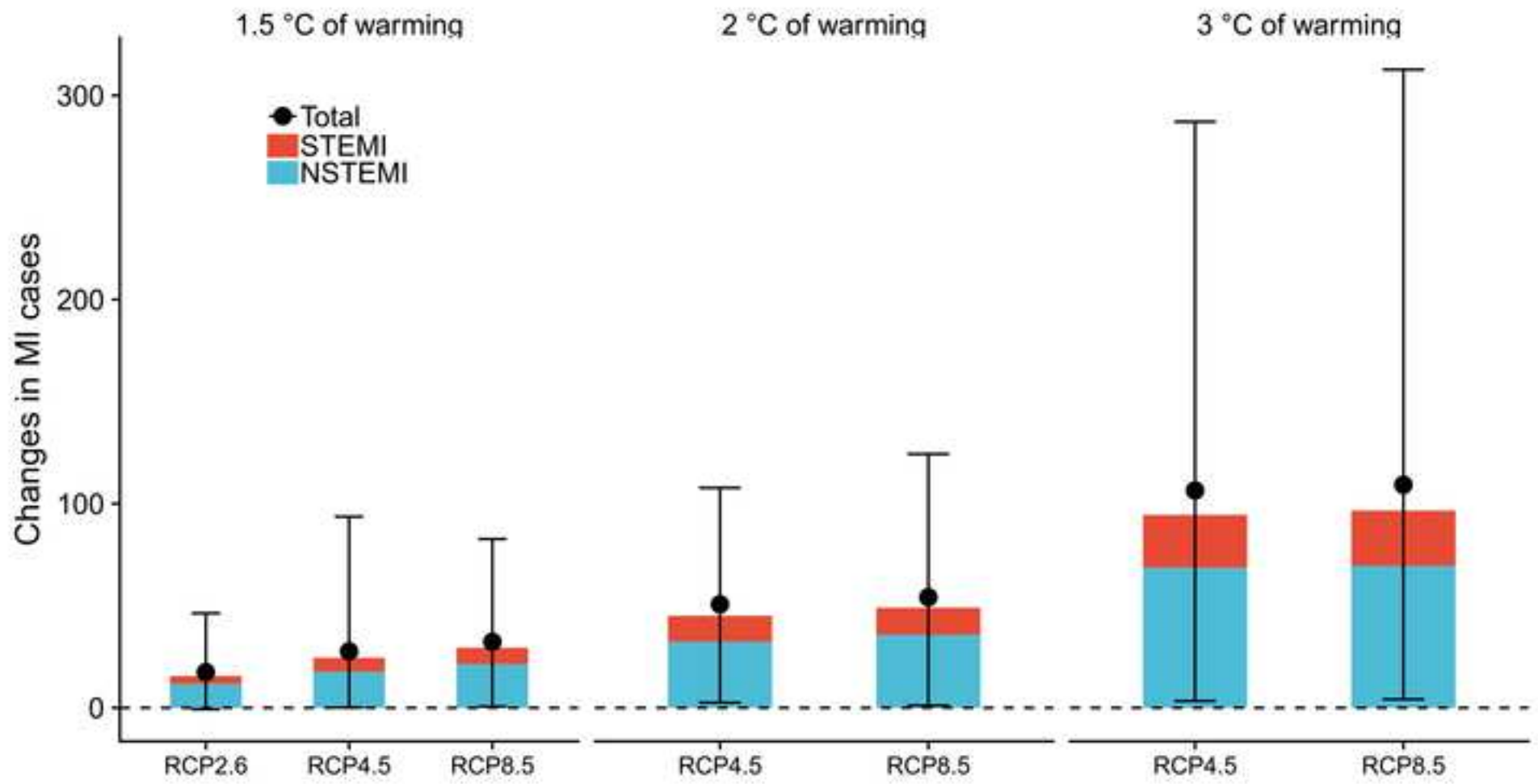
* Based on the average of 4 global climate models, i.e., GFDL-ESM2M, HadGEM2-ES, IPSL-CM5A-LR and MIROC5.

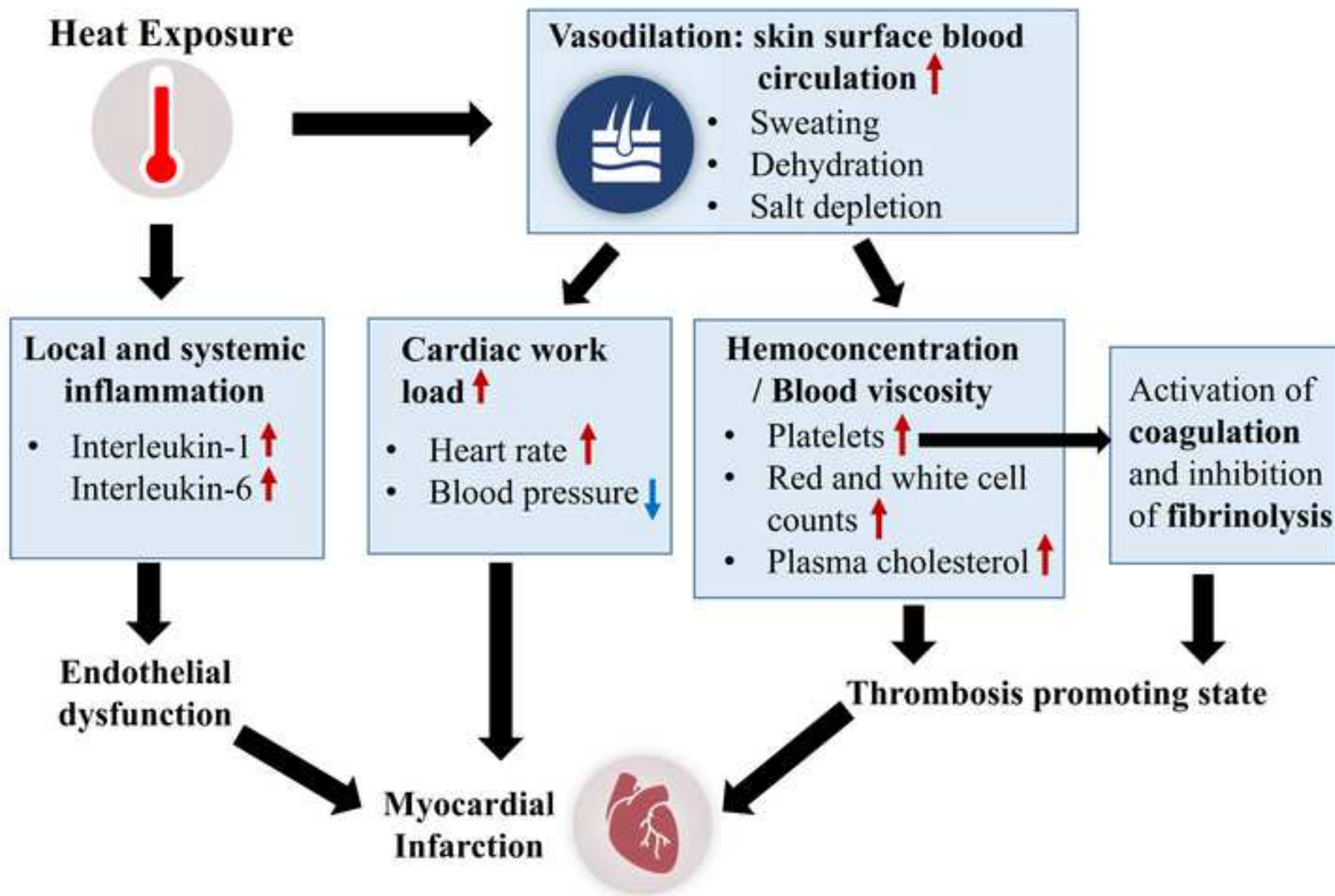
Table 2. Changes in attributable number and fraction (95% eCIs) of heat-related MI cases per decade in Augsburg under 1.5 °C, 2 °C, and 3 °C of global warming.*

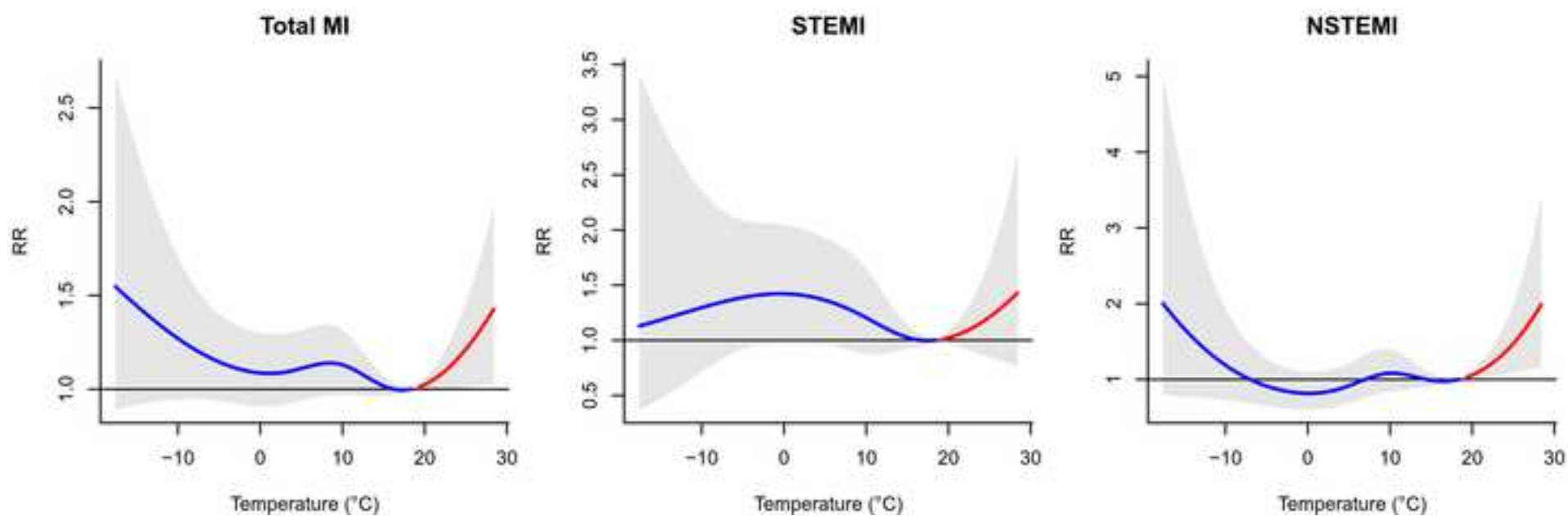
Warming	RCP	Attributable number			Attributable fraction (%)		
		Total	STEMI	NSTEMI	Total	STEMI	NSTEMI
1.5 °C	RCP2.6	17 (-1, 46)	4 (-4, 15)	12 (2, 27)	0.2 (0, 0.5)	0.2 (-0.2, 0.6)	0.4 (0, 0.8)
	RCP4.5	28 (0, 94)	7 (-8, 29)	18 (1, 53)	0.3 (0, 1.0)	0.3 (-0.3, 1.2)	0.5 (0, 1.6)
	RCP8.5	32 (1, 83)	8 (-8, 25)	21 (4, 48)	0.3 (0, 0.9)	0.3 (-0.4, 1.1)	0.6 (0.1, 1.5)
2.0 °C	RCP2.6	-	-	-	-	-	-
	RCP4.5	51 (3, 108)	13 (-13, 35)	32 (7, 60)	0.5 (0, 1.1)	0.5 (-0.5, 1.5)	1 (0.2, 1.8)
	RCP8.5	54 (1, 124)	13 (-14, 39)	36 (7, 72)	0.6 (0, 1.3)	0.6 (-0.6, 1.7)	1.1 (0.2, 2.2)
3.0 °C	RCP2.6	-	-	-	-	-	-
	RCP4.5	106 (3, 287)	26 (-25, 89)	69 (14, 163)	1.1 (0, 3.0)	1.1 (-1.1, 3.8)	2.1 (0.4, 4.9)
	RCP8.5	109 (4, 313)	27 (-27, 97)	70 (11, 171)	1.1 (0, 3.2)	1.2 (-1.2, 4.1)	2.1 (0.3, 5.2)

* 95% eCIs were obtained by considering the uncertainty of concentration-response function using 5000 times of Monte Carlo simulations and four global climate models. The decades when 1.5 °C, 2.0 °C, and 3.0 °C of global warming are projected to be reached vary among RCPs, see Table 1.









eBox: Key elements in the climate change impact assessment

- The expose-response curves were obtained from a previous research (3);
- We assume a constant population (size, age structure, and lifestyle);
- We assume a constant incidence for the total number and subtypes of MI;
- The temperature projections for the Augsburg region were obtained from 4 global climate models under 3 different climate change scenarios;
- Projection uncertainty source includes both the uncertainty of exposure-response curves and the variability across 4 climate models

eMethods

Study population

We collected data from the population-based Cooperative Health Research in the Region of Augsburg (KORA) MI registry. The Augsburg region includes the city of Augsburg (with an area of 147 km²) and the two adjacent rural counties (1,854 km²). The MONICA/KORA MI registry was founded in 1984 as part of the WHO MONICA (Monitoring Trends and Determinants in Cardiovascular Disease) project and since 1996 has been continued as part of the KORA research program. Since 1984, all cases of MI in eight hospitals in the study area and coronary deaths occurring among residents aged 25 to 74 years old (about 400,000 inhabitants) have been continuously registered in the MONICA/KORA MI registry. Following the MONICA protocol, MI patients who survived at least 24 hours after hospitalization are interviewed about the event, demographic information, co-morbidities, medication, and family history. If a patient survives the 28th day after hospital admission, the MI is identified as nonfatal, otherwise as fatal. Coronary deaths are fatal cases outside the hospital or within the 24-hour after admission to a hospital. All coronary deaths (ICD-9 codes: 410-414) were identified by checking all death certificates through the regional health departments and by information from the last treating physician and/or coroner.

In this study, we used all recorded cases of MI and coronary deaths among residents aged 25 to 74 from January 1, 2001, to December 31, 2014. We further analyzed subtypes of MI events including ST-segment elevation MI (STEMI) and non-ST segment elevation MI (NSTEMI) events. Bundle branch block was not included in this analysis due to its small sample size (38.6 cases/year). More details of this registry can be found elsewhere (1, 2).

Exposure-response functions and baseline MI

We applied estimates of the exposure-response functions (ERFs) between daily mean temperature and daily MI events from our previous work for the period 2001-2014 (3). Briefly, we conducted a time-stratified case-crossover study and used a distributed lag nonlinear model with a maximum lag of 10 days to estimate the ERFs. Temperature and MIs generally showed U-shaped associations, with significant increasing risks for heat [temperatures above the minimum MI temperature (MMIT, as the reference temperature, 18.4 °C)] but non-significant increasing risk for cold (temperatures below the MMIT) (*eFigure 1*). The baseline MI cases were calculated as the average observed number of cases for each day of the year during 2001-2014.

Temperature projections

We obtained daily mean temperature projections during 2010-2099 from the Inter-Sectoral Impact Model Intercomparison Project Phase 2b (ISIMIP2b) (4). We used three climate change scenarios under the Representative Concentration Pathway (RCP) 2.6, RCP4.5, and RCP8.5, corresponding to low, moderate, and high warming and emission scenarios, respectively. We obtained daily temperature simulations at a spatial resolution of $0.5^\circ \times 0.5^\circ$ from all four global climate models (GCMs) included in ISIMIP2b (i.e., GFDL-ESM2M, HadGEM2-ES, IPSL-CM5-IL, and MIROC5). These temperature simulations have been bias-corrected based on the EWEMBI dataset (5). As applied in previous studies (6, 7), we obtained daily temperatures in the baseline and future periods by extracting the temperature projections in one grid cell that covers the geographical center of the Augsburg area.

To determine the period when 1.5 °C, 2 °C, and 3 °C of warming above pre-industrial levels will be reached, we applied the method described in Ebi et al. (2018) (8) in support of the IPCC Special Report on the impacts of global warming of 1.5 °C. We first defined the baseline period as the decade 2010-2019, as its center year 2015 is the first year reaching 1 °C above pre-industrial levels (defined as the average of 1850-1900) (8). We then created a series of 10-year moving average projection windows, starting from 2011-2020 with a one-year step. We thus selected decade windows for each RCP when the GCM-ensemble average of global mean near-surface air temperature reached 0.5 °C, 1 °C, and 2 °C above the 2010-2019 baseline.

Health impact assessment

We estimated the number and fraction of MI cases attributable to heat exposure in baseline and future periods under the assumption of no future changes in population and adaptation, using a recently developed approach (9). Briefly, we applied the previously estimated ERFs (3) and the modeled daily series of temperature and MI to calculate the daily attributable number of MI cases. We then calculated the total attributable number by summing the contributions from all the days of the series and calculated the attributable fraction as the ratio of the total attributable number to the total number of MI cases. Finally, we computed the future changes as the differences between the future periods and the baseline period for each GCM and each RCP.

We computed the GCM-ensemble average total attributable number and fractions of MI cases by combinations of RCPs and future periods corresponding to warmings of 1.5 °C, 2 °C and 3 °C. We used Monte Carlo simulations to estimate empirical confidence interval (eCI) to

address the uncertainty in ERF and the variability across GCMs. We obtained eCI from the empirical distribution across 5,000 samples of random parameter sets describing the ERF in the distributed lag nonlinear model and four GCMs, as described in more detail elsewhere (6, 9). Briefly, we quantified the uncertainty in ERF by generating 5,000 samples through Monte Carlo simulations for the estimated coefficients in the distributed lag nonlinear model which estimated the ERF. We then generated results for each of the four GCMs. We obtained the 95% eCI, defined as the 2.5th - 97.5th percentiles of empirical distribution across ERF coefficients samples and GCMs. Thus, the 95% eCI account for both the ERF and GCM sources of uncertainty.

References

1. Löwel H, Meisinger C, Heier M, Hörmann A: The population-based acute myocardial infarction (AMI) registry of the MONICA/KORA study region of Augsburg. *Das Gesundheitswesen* 2005; 67: 31-7.
2. Kuch B, Heier M, Von Scheidt W, Kling B, Hoermann A, Meisinger C: 20-year trends in clinical characteristics, therapy and short-term prognosis in acute myocardial infarction according to presenting electrocardiogram: the MONICA/KORA AMI Registry (1985–2004). *J Intern Med* 2008; 264: 254-64.
3. Chen K, Breitner S, Wolf K, et al.: Temporal variations in the triggering of myocardial infarction by air temperature in Augsburg, Germany, 1987-2014. *Eur Heart J* 2019.
4. Frieler K, Lange S, Piontek F, et al.: Assessing the impacts of 1.5 °C global warming – simulation protocol of the Inter-Sectoral Impact Model Intercomparison Project (ISIMIP2b). *Geosci Model Dev* 2017; 10: 4321-45.
5. Lange S: Bias correction of surface downwelling longwave and shortwave radiation for the EWEMBI dataset. *Earth Syst Dynam* 2018; 9: 627-45.
6. Gasparrini A, Guo Y, Sera F, et al.: Projections of temperature-related excess mortality under climate change scenarios. *Lancet Planet Health* 2017; 1: e360-e7.
7. Weinberger KR, Kirwa K, Eliot MN, Gold J, Suh HH, Wellenius GA: Projected changes in temperature-related morbidity and mortality in Southern New England. *Epidemiology* 2018; 29: 473-81.
8. Ebi KL, Hasegawa T, Hayes K, Monaghan A, Paz S, Berry P: Health risks of warming of 1.5° C, 2° C, and higher, above pre-industrial temperatures. *Environ Res Lett* 2018; 13: 063007.
9. Gasparrini A, Leone M: Attributable risk from distributed lag models. *BMC Med Res Methodol* 2014; 14: 55.