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Supplemental Material

Changing Susceptibility to Non-Optimum Temperatures in Japan, 1972-2012: The Role of Climate, Demographic, and Socioeconomic Factors

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Table of Contents

Figure S4. Region-specific time-varying minimum mortality temperature (MMT) together with the time-varying minimum mortality temperature percentile (MMTP) (top), time-varying heat-related mortality risk (middle), and time-varying cold-related mortality risk (bottom). Black solid and dashed lines indicate the point estimate of the MMT and 95% point-wise confidence intervals, respectively. Blue line in the top panels indicates the MMTP.

Figure S5. Prefecture-specific time-varying minimum mortality temperature (MMT) and minimum mortality temperature percentile (MMTP). Black solid and dashed lines indicate the point estimate of the MMT and 95% point-wise confidence intervals, respectively. Blue line indicates the MMTP.

Figure S6. Prefecture-specific time-varying heat-related mortality risk. The heat-related risk was defined as the relative risk comparing the time-varying minimum mortality temperature (MMT) and the time-varying 99^{th} temperature percentile. Black solid and dashed lines indicate the point estimate of the heat risk and 95% point-wise confidence intervals, respectively.

Figure S7. Prefecture-specific time-varying cold-related mortality risk. The cold-related risk was defined as the relative risk comparing the time-varying minimum mortality temperature (MMT) and the time-varying 1^{st} temperature percentile. Black solid and dashed lines indicate the point estimate of the heat risk and 95% point-wise confidence intervals, respectively.

Figure S8. Prefecture-specific lag-cumulative relative risk (RR) curve at the first/last years (1972/2012) of the study period. Green and blue sold lines with shaded areas indicate the estimated RR curves with 95% confidence regions in 1972 and in 2012, respectively.

Figure S9. Gender-specific time-varying minimum mortality temperature (MMT) together with the time-varying minimum mortality temperature percentile (MMTP) (top), time-varying heat-related mortality risk (middle), and time-varying cold-related mortality risk (bottom). Black solid and dashed lines indicate the point estimate of the MMT and 95% point-wise confidence intervals, respectively. Blue line in the top panels indicates the MMTP.

Figure S10. Cause-specific time-varying minimum mortality temperature (MMT) together with the time-varying minimum mortality temperature percentile (MMTP) (top), time-varying heat-related mortality risk (middle), and time-varying cold-related mortality risk (bottom). Black solid and dashed lines indicate the point estimate of the MMT and 95% point-wise confidence intervals, respectively. Blue line in the top panels indicates the MMTP.

Details for statistical methods

Two-stage modeling

The first stage models the time-varying association between temperature and mortality for each prefecture. For i-th prefecture, let y_{it} be the daily death count on day t, $\mathbf{x}_{it} = (x_{it}, x_{it-1}, \dots, x_{it-L})'$ be the vector of daily mean temperatures on day t and over the previous L days and T_t be a variable representing time on day t. We use the following generalized linear model with a quasi-Poisson family.

$$y_{it} \sim \text{quasi-Poisson}(\lambda_{it}),$$

$$log(\lambda_{it}) = \alpha_{i0} + s_i(\mathbf{x}_{it}, T_t; \boldsymbol{\beta}_i) + \sum_{j=1}^{J} h_{ij}(u_{ijt}; \boldsymbol{\gamma}_{ij}), \text{ for } t = L+1, \dots, N, \qquad (1)$$

where $\lambda_{it} \equiv \mathrm{E}(y_{it})$ is the expected mortality count for i-th prefecture on day t, α_{i0} is a model intercept, u_{ijt} is j-th control variable for i-th prefecture on day t, $h_{ij}(\cdot)$ is a flexible function to represent the effect of j-th control variable for i-th prefecture, characterized by $\boldsymbol{\gamma}_{ij}$. In our analysis, $h_{ij}(\cdot)$ include a natural cubic B-spline of time with 8 degrees of freedom (df) per year to control for seasonality and long-term time trend and indicator variables to control for the day of week.

In equation (1), $s_i(\cdot)$ is a flexible function to describe a time-varying, nonlinear and delayed association between temperature and mortality, and we use a time-varying distributed lag nonlinear model (TV-DLNM) as follows. We first define a cross-basis (CB) for temperature and lag as in the time-constant DLNM. Let $f_1(\cdot), \cdots, f_{v_x}(\cdot)$ be the basis to describe the nonlinear temperature-mortality association with dimension v_x and let $g_1(\cdot), \cdots, g_{v_l}(\cdot)$ be the basis to describe the relationship along the lag space. Then, the TV-DLNM for $s_i(\cdot)$ is expressed as follows

$$s(\mathbf{x}_{it}, T_t; \boldsymbol{\beta}_i) = \sum_{j=1}^{v_x} \sum_{k=1}^{v_l} \mathbf{r}'_{i,tj\cdot} \mathbf{c}_{\cdot \mathrm{k}} \beta_{i,jk0} + T_t \sum_{j=1}^{v_x} \sum_{k=1}^{v_l} \mathbf{r}'_{i,tj\cdot} \mathbf{c}_{\cdot \mathrm{k}} \beta_{i,jk1} \qquad (2)$$

where $\mathbf{r}_{i,tj} = \left(f_j(x_{it}), \cdots, f_j(x_{it-L})\right)'$ is the transformed vector using j-th basis f_j in the temperature dimension and $\mathbf{c}_{\cdot \mathrm{k}} = (g_k(0), \cdots, g_k(L))'$ is the transformed vector using k-th basis $\mathrm{g_k}$ in the lag dimension. The coefficient vector $\boldsymbol{\beta}_i = \left(\beta_{i,110}, \beta_{i,120,} \dots, \beta_{i,v_x v_l 1}\right)'$ has the length of $v_x \times v_l \times 2$ and is divided into the coefficients for the main term of the CB, $\boldsymbol{\beta}_i =$

$\left(\beta_{i,110}, \beta_{i,120,} \dots, \beta_{i,v_x v_l 0}\right)'$ and the coefficients for the interaction between the CB and time, $\boldsymbol{\beta}_i = \left(\beta_{i,111}, \beta_{i,121,} \dots, \beta_{i,v_x v_l 1}\right)'$, with the length of $v_x \times v_l$ for each. In our analysis, we use a quadratic B-spline for temperature with three internal knots and a natural cubic spline for the lag with three internal knows and thus, $v_x = 5$ and $v_l = 5$. Therefore, the coefficients in $s_i(\cdot)$ are $5\times 5 \times 2$=50.

Because of the high dimensionality, we reduce the coefficients over the lag space as follows.

$$\boldsymbol{\theta}_i = \mathbf{M_1}\boldsymbol{\beta}_i$$

$$V(\boldsymbol{\theta}_i) = \mathbf{M_1} V(\boldsymbol{\beta}_i)\mathbf{M_1'} \qquad (3)$$

where $\boldsymbol{\beta}_i$ is the set of 50 coefficients, $\mathbf{M_1} = \mathbf{I}_{2\times v_x} \otimes \mathbf{1}'_{L+1}\mathbf{C}$ is a reducing matrix, $\boldsymbol{\theta}_i = \left(\theta_{i,1,0}, \theta_{i,2,0} \dots, \theta_{i,v_x,1}\right)'$ is the set of reduced coefficient with length of $v_x \times 2$, and $V(\boldsymbol{\theta}_i)$ is the associated error covariance matrix. The $\boldsymbol{\theta}_i$ is divided into the ones for the main term, $\boldsymbol{\theta}_i = \left(\theta_{i,1,0}, \theta_{i,2,0} \dots, \theta_{i,v_x,0}\right)'$ and the ones for the interaction, $\boldsymbol{\theta}_i = \left(\theta_{i,1,1}, \theta_{i,2,1} \dots, \theta_{i,v_x,1}\right)'$ with length of v_x for each. In our analysis, as $v_x = 5$, the reduced set of coefficients $\boldsymbol{\theta}_i$ include 10 coefficients, 5 for the main term and 5 for the interaction. The 10 coefficients represent the time-varying temperature-mortality association cumulated over the lags. Then, in the second stage, we apply a multivariate meta-analysis using the 10 coefficients and their standard error matrices obtained from the first stage modeling and obtain a pooled estimate and the best linear unbiased predictor (BLUP) for $\boldsymbol{\theta}_i$ and its error matrices.

Estimating the time-varying MMT, heat- and cold-related mortality risks

Let $\widehat{\boldsymbol{\theta}_i}$ be the BLUP and $V\left(\widehat{\boldsymbol{\theta}_i}\right)$ be the corresponding error matrix. Using them, we first estimate the time-varying MMT over a grid of every 10 days for the whole study period. Let T_t represent a specific time point. Then, the MMT at that time point, denoted by MMT_{T_t}, can be derived as follows.

$$\widehat{\boldsymbol{\eta}_{i,x}} = \mathbf{M}_{\mathbf{2},x}\widehat{\boldsymbol{\theta}}_i = (\widehat{\eta_{i,x,0}}, \quad \widehat{\eta_{i,x,1}})'$$

$$MMT_{T_t} = argmin_x(\widehat{\eta_{i,x,0}} + T_t \times \widehat{\eta_{i,x,1}}) \qquad (4)$$

where $\mathbf{M}_{\mathbf{2},x} = \mathbf{I}_2 \otimes \mathbf{q}'_x$ is the reducing matrix and $\mathbf{q}_x$ is the vector of a specific temperature x transformed through the basis for temperature. However, the solution in (4) serves as a point estimate only and a confidence interval cannot be calculated. Therefore, we use a Monte Carlo simulation method (ref) to obtain the empirical distribution of the MMT at a given time T_t. We first simulate $\boldsymbol{\theta}_i{}'s$ from a multivariate normal distribution with mean as the BLUP and the covariance as the standard error matrix and calculate the MMT for each simulated $\boldsymbol{\theta}_i$ in the same way as in (4) . The procedure is expressed as follows.

$$\boldsymbol{\theta}_{i,(j)} \sim N(\widehat{\boldsymbol{\theta}}_i, V(\widehat{\boldsymbol{\theta}}_i))$$

$$\boldsymbol{\eta}_{i,(j),x} = \boldsymbol{M}_{\mathbf{2},x}\boldsymbol{\theta}_{i,(j)}$$

$$MMT_{T_t,(j)} = argmin_x(\eta_{i,(j),x,0} + T_t \times \eta_{i,(j),x,1}) \quad (5)$$

where (j) indicates j-th simulated sample. We obtain 1,500 samples of the MMT_{T_t} through the procedure (5) and use the sample mean as a point estimate and the sample 2.5th and 97.5th percentiles as an interval estimate for the MMT.

Next, we estimate the time-varying heat- and cold-related mortality risks over a grid of every 10 days for the whole study period. At a specific time point T_t, the heat- and cold-related mortality risks are calculated as follows.

$$\text{Heat Risk}_{T_t} = \exp\{(1, T_t) \times \left(\mathbf{M}_{\mathbf{2},\mathrm{x}_{\text{heat},T_t}}\widehat{\boldsymbol{\theta}}_i - \mathbf{M}_{\mathbf{2},MMT_{T_t}}\widehat{\boldsymbol{\theta}}_i\right)\}$$

$$\text{Cold Risk}_{T_t} = \exp\{(1, T_t) \times \left(\mathbf{M}_{\mathbf{2},\mathrm{x}_{\text{cold},T_t}}\widehat{\boldsymbol{\theta}}_i - \mathbf{M}_{\mathbf{2},MMT_{T_t}}\widehat{\boldsymbol{\theta}}_i\right)\} \qquad (6)$$

where x_{heat,T_t} and x_{heat,T_t} are the 99th and the 1st percentile, respectively, of the temperature distribution at a specific time T_t. Also, pointwise confidence intervals were calculated through the corresponding transformation of $V(\widehat{\boldsymbol{\theta}}_i)$.

Investigating the relation with prefecture-specific meta-variables

Let y_{ij} be ith prefecture's estimated aspect (MMT, heat or cold risks) at time point j. The logged values of RR were used as y_{ij} for the heat and cold risks. Let x_{ij} be ith prefecture's meta-variable observed at time j. Then, for each aspect and each meta-variable, we fit the following linear mixed effects model (LMEM). For i=1,..,46 (excluding Okinawa) and j=1,…, T (T is the number of yearly time points and ranges from 8 to 41 depending on the meta-variable),

$$E(y_{ij}) = \alpha_{i0} + \mathrm{x}_{ij}\alpha_1 + f_i(\mathrm{Time}_{ij}; \boldsymbol{\beta}_i) + longitude_i + latitude_i + \mathrm{e}_{ij}, \qquad (7)$$

where α_{i0} is ith prefecture-specific intercept (a combination of fixed intercept and random intercept), Time_{ij} represents the time at jth time point for ith prefecture (the years for which each meta-variable is available), $f_i(\cdot)$ is a flexible function characterized by $\boldsymbol{\beta}_i$ to adjust for prefecture-specific nonlinear time trends, and e_{ij} are residuals with a 1st order autoregressive (AR(1)) within-prefecture residual correlation structure. For $f_i(\cdot)$, we used natural cubic spline with two internal knots placed at 1985 and 2000 for all meta-variables except for EPI. For EPI, we used a linear function because the yearly measurements were available only after 2003. Then, α_1 represents the association between each aspect and each meta-variable, as the change in MMT, or in the log of heat/cold risks per unit change in each meta-variable. Each-meta variable was properly scaled such that the estimate for α_1 is not a value too close to zero. For fitting model (7) and estimating α_1, we used the maximum likelihood estimation with weights given for y_{ij} as an inverse of the squared standard error for the estimated aspect to incorporate uncertainty.

Table S1. Summary statistics for daily mortality and mean temperature (study period: 1972.01.01 - 2012.12.31 for Hokkaido-Nagasaki, 1973.01.01 - 2012.12.31 for Okinawa)

Region	Prefecture name	Latitude (⁰ N)	Longitude (⁰ E)	Total deaths	Average daily deaths	Distribution of daily mean temperature (°C)						
						Min	1st	25th	50th	75th	99th	Max
East	Hokkaido	43.06	141.35	1636834	109.3	-14.1	-8.3	0.1	9.2	17.2	25.9	30.1
East	Iwate	39.70	141.15	487277	32.5	-8.9	-6.2	1.6	10.3	18.3	27.0	29.6
East	Miyagi	38.27	140.87	638639	42.6	-5.2	-2.1	4.8	12.8	19.1	27.8	31.2
East	Aomori	40.82	140.74	495285	33.1	-8.7	-5.3	2.1	10.6	17.9	27.0	30.1
East	Fukushima	37.75	140.47	711527	47.5	-5.2	-2.2	4.8	13.3	20.2	29.1	31.4
East	Ibaraki	36.34	140.45	855768	57.1	-3.8	-0.2	6.1	14.1	20.2	28.4	31.3
East	Yamagata	38.24	140.36	458516	30.6	-7.4	-4.1	3.0	11.9	19.7	28.2	31.5
East	Chiba	35.60	140.12	1335634	89.2	-1.4	2.0	8.6	16.1	22.0	29.3	32.2
East	Akita	39.72	140.10	450848	30.1	-6.4	-3.7	3.3	11.6	19.6	28.2	31.6
East	Tochigi	36.57	139.88	597355	39.9	-4.5	-1.0	5.8	14.3	20.8	28.7	31.4
East	Tokyo	35.69	139.69	3056617	204.1	-0.6	2.6	9.0	16.5	22.5	30.1	33.1
East	Saitama	35.86	139.65	1437142	96.0	-2.8	0.7	7.1	15.3	21.8	30.1	33.7
East	Kanagawa	35.45	139.64	1785316	119.2	-1.0	2.4	8.8	16.1	21.9	29.0	30.9
East	Gunma	36.39	139.06	612478	40.9	-3.8	0.0	6.7	14.8	21.5	29.9	32.6
East	Niigata	37.90	139.02	844622	56.4	-3.9	-0.9	5.8	13.9	21.2	29.5	32.6
East	Yamanashi	35.66	138.57	287196	19.2	-4.4	-0.4	6.5	15.1	22.1	29.1	31.8
East	Shizuoka	34.98	138.38	1052669	70.3	-0.9	3.2	9.9	17.0	22.7	29.2	31.9
East	Nagano	36.65	138.18	741340	49.5	-7.7	-4.3	3.0	12.4	20.3	28.	30.7
East	Toyama	36.70	137.21	379473	25.3	-4.4	-1.3	6.1	14.3	21.3	29.8	33.8
East	Aichi	35.18	136.91	1683493	112.4	-2.9	0.8	7.9	16.2	22.9	30.3	32.7
East	Gifu	35.39	136.72	626398	41.8	-3.0	0.6	7.9	16.2	23.1	30.5	32.9
East	Ishikawa	36.59	136.63	365554	24.4	-3.9	-0.4	6.9	14.9	21.8	29.7	32.3
West	Mie	34.73	136.51	587047	39.2	-2.4	1.6	8.3	16.1	22.8	30.2	33.5
East	Fukui	36.07	136.22	242150	18.2	-3.8	-0.3	6.4	14.9	22.0	30.0	32.1
West	Shiga	35.00	135.87	354703	23.7	-3.2	0.1	6.8	14.8	22.0	29.4	31.4
West	Nara	34.69	135.83	388331	25.9	-3.7	0.5	6.9	15.1	22.1	29.1	31.7
West	Kyoto	35.02	135.76	772252	51.6	-3.4	1.1	7.9	16.2	23.2	30.5	32.8
West	Osaka	34.69	135.52	2276669	152.0	-2.1	2.4	9.1	17.2	23.9	30.8	32.9
West	Hyogo	34.69	135.18	1587308	106.0	-4.3	1.3	8.8	16.8	23.2	29.9	32.0
West	Wakayama	34.23	135.17	398680	26.6	-2.7	2.6	9.1	17.0	23.5	29.9	31.9
West	Tokushima	34.07	134.56	309974	20.7	-4.0	2.3	9.2	17.0	23.3	29.8	32.3
West	Tottori	35.50	134.24	226586	15.1	-5.6	0.1	7.3	15.0	21.9	29.9	32.3
West	Kagawa	34.34	134.04	355744	23.8	-3.3	2.0	8.5	16.4	23.2	30.5	32.3

West	Okayama	34.66	133.94	652830	43.6	-4.8	0.8	7.9	16.2	23.2	30.6	32.3
West	Kochi	33.56	133.53	332332	22.2	-2.3	2.2	10.1	17.6	23.6	29.4	32.1
West	Shimane	35.47	133.05	309673	20.7	-5.3	0.4	7.5	15.0	21.6	29.4	32.2
West	Ehime	33.84	132.77	539865	36.0	-3.1	2.1	9.1	16.6	23.1	29.8	31.9
West	Hiroshima	34.40	132.46	883124	59.0	-5.8	1.1	8.3	16.2	23.0	30.2	32.7
West	Oita	33.24	131.61	440295	29.4	-3.4	2.3	9.4	16.7	22.9	29.6	31.6
West	Yamaguchi	34.19	131.47	573274	38.3	-5.4	0.4	7.7	15.7	22.6	29.3	31.2
West	Miyazaki	31.91	131.42	390734	26.1	-1.0	3.3	11.0	18.1	23.8	29.9	32.0
West	Kumamoto	32.79	130.74	631598	42.2	-3.2	1.3	9.5	17.5	24.0	30.2	31.5
West	Kagoshima	31.56	130.56	686996	45.9	-2.1	3.6	12.0	18.9	24.8	30.1	31.1
West	Fukuoka	33.61	130.42	1447571	96.7	-3.2	2.4	9.9	17.1	23.3	305	32.4
West	Saga	33.25	130.30	309797	20.7	-3.6	1.5	9.2	16.9	23.6	30.0	32.2
West	Nagasaki	32.74	129.87	538568	36.0	-2.5	2.5	10.5	17.6	23.5	29.7	32.2
West	Okinawa	26.21	127.68	282393	19.3	9.1	12.9	19.2	23.3	27.2	30.0	31.1

Table S2. Prefecture-specific average of yearly measurements for each meta-variable

Region	Prefecture Name	Climate variable [a]				Demographic variable [b]			Socio-economic variable [c]			AC [d] prevalence (%)
		Tmax (°C)	Tmean (°C)	Tmin (°C)	RHmean (%)	%4- (%)	%5-9 (%)	%65+ (%)	Savings (million yen)	CPI (unit)	EPI (%)	
East	Hokkaido	26.86	8.82	-9.33	66.67	5.56	6.02	14.52	7.90	85.21	0.38	6.14
East	Iwate	27.26	10.20	-6.76	73.84	1.39	6.18	16.93	7.99	83.59	0.29	20.36
East	Miyagi	28.80	12.36	-3.00	71.13	2.21	6.21	14.01	8.25	84.72	0.51	33.43
East	Aomori	27.57	10.28	-6.31	74.81	1.46	6.39	15.39	6.71	80.67	0.30	18.90
East	Fukushima	29.63	12.97	-2.99	68.91	2.05	6.38	16.35	8.40	82.47	0.42	33.86
East	Ibaraki	28.93	13.62	-0.72	74.47	2.76	6.44	14.12	10.63	83.18	0.60	53.20
East	Yamagata	28.93	11.67	-4.73	74.48	1.23	5.87	18.26	8.22	83.51	0.31	38.91
East	Chiba	29.58	15.67	-1.36	68.68	5.34	6.44	12.08	10.97	85.10	0.72	63.12
East	Akita	29.17	11.65	-4.58	73.09	1.20	5.66	18.27	7.42	84.23	0.27	30.72
East	Tochigi	29.00	13.71	-1.43	69.85	1.89	6.39	14.26	11.06	82.76	0.58	54.73
East	Tokyo	30.72	16.19	1.72	62.07	12.06	5.14	12.65	12.88	85.96	1.21	74.09
East	Saitama	30.46	14.89	-0.02	65.68	6.19	6.63	11.03	10.53	84.07	0.70	72.88
East	Kanagawa	29.42	15.74	-1.58	67.15	7.80	6.12	11.36	12.39	84.38	0.89	65.44
East	Gunma	30.28	14.49	-0.80	63.54	1.93	6.32	15.14	10.63	85.17	0.55	58.94
East	Niigata	30.40	13.76	-1.52	71.77	2.43	6.01	17.24	9.97	83.99	0.40	57.84
East	Yamanashi	29.31	14.54	-1.27	65.30	0.84	6.15	16.59	9.79	83.21	0.38	42.05
East	Shizuoka	29.91	16.55	2.22	67.76	3.60	6.34	14.58	11.17	83.46	0.70	58.08
East	Nagano	28.58	11.88	-5.01	72.12	2.13	6.09	17.85	10.63	84.68	0.44	27.96
East	Toyama	30.70	13.98	-2.11	77.35	1.10	5.91	17.08	11.28	85.02	0.42	62.83
East	Aichi	30.46	15.70	-0.23	66.69	6.68	6.46	12.07	12.45	84.68	0.97	73.91
East	Gifu	30.77	15.74	-0.42	67.30	2.02	6.35	15.10	11.78	84.52	0.49	61.70
East	Ishikawa	30.50	14.59	-1.16	71.95	1.14	6.22	15.65	11.97	85.95	0.44	62.88
West	Mie	30.61	15.79	0.59	69.00	1.77	6.20	15.91	11.82	82.06	0.54	68.16
East	Fukui	30.56	14.51	-1.02	75.11	0.81	6.25	16.87	12.80	85.25	0.38	67.39
West	Shiga	29.54	14.63	-0.77	74.18	1.22	6.65	13.95	11.95	84.20	0.53	67.06
West	Nara	29.44	14.82	-0.39	72.75	1.31	6.25	14.42	12.46	85.99	0.39	75.27
West	Kyoto	30.68	15.83	-0.08	66.19	2.56	5.85	14.93	11.06	82.57	0.56	78.23
West	Osaka	31.02	16.78	1.35	63.63	8.62	6.14	12.48	10.79	84.57	0.75	82.62
West	Hyogo	30.12	16.25	0.17	66.45	5.34	6.24	14.25	11.62	85.37	0.55	73.09
West	Wakayama	30.25	16.57	1.51	66.37	1.06	6.03	17.65	10.75	84.38	0.30	69.89
West	Tokushima	30.15	16.46	0.81	66.84	0.81	5.77	17.96	10.75	84.97	0.31	65.83
West	Tottori	30.44	14.82	-1.19	73.81	0.60	6.04	18.09	10.54	84.50	0.25	59.16
West	Kagawa	30.52	16.12	0.90	68.44	1.00	5.95	17.42	12.55	84.38	0.43	74.12

West	Okayama	30.54	15.85	-0.21	68.36	1.90	6.08	16.99	11.55	83.97	0.48	70.85
West	Kochi	29.66	16.87	1.13	68.47	0.81	5.67	19.53	9.53	84.71	0.23	57.90
West	Shimane	29.73	14.81	-1.08	75.88	0.76	5.87	20.23	9.66	82.93	0.23	56.21
West	Ehime	30.16	16.32	0.75	66.60	1.48	6.08	17.62	9.70	84.44	0.37	61.71
West	Hiroshima	30.10	15.88	-0.42	69.40	2.80	6.19	15.47	10.77	84.89	0.54	69.27
West	Oita	29.98	16.31	0.93	70..03	1.21	6.06	17.76	8.13	84.55	0.33	56.01
West	Yamaguchi	29.40	15.30	-1.13	73.61	1.54	5.88	18.13	9.96	86.46	0.41	61.49
West	Miyazaki	30.37	17.49	2.22	73.72	1.14	6.53	16.69	6.75	85.05	0.29	54.65
West	Kumamoto	30.39	16.79	0.11	70.79	1.81	6.18	17.47	7.65	84.44	0.36	60.83
West	Kagoshima	30.24	18.30	2.14	70.59	1.76	6.29	18.48	6.66	83.23	0.29	53.38
West	Fukuoka	30.75	16.85	0.97	68.09	4.77	6.16	14.40	8.60	85.08	0.58	69.69
West	Saga	30.21	16.49	0.19	70.81	0.86	6.49	16.97	8.44	85.73	0.31	65.87
West	Nagasaki	30.17	17.09	1.01	70.51	1.53	6.54	16.83	7.36	83.56	0.27	59.16
West	Okinawa	29.89	22.91	11.84	74.42	1.24	8.11	11.89	4.09	91.12	0.28	59.88

[a] Climate variables for 1972–2012 (annual values, N = 41): Tmax (maximum daily mean temperature), Tmean (average daily mean temperature), Tmin (minimum daily mean temperature) and RHmean (average daily mean relative humidity)

[b] Demographic variables for 1972–2012 (annual values, N = 41): Percent of population ≤ 4, 5–9, and ≥ 65 years of age.

[c] Socio-economic variables: Savings (annual average savings per household with two or more persons, available every 5 years from 1974–2009, N = 8), EPI (economic power index, a measure of financial strength of a local government, higher value represents more strength, 2003-2010, N =8), CPI (consumer price index, measure of the cost of goods and services by household, 1972-2012, N = 41)

[d] Air conditioning prevalence for households with two or more persons, 1972-2009 (N = 38)

Table S3. Association between each aspect (MMT, heat- and cold-related mortality risks) and each meta-variable in female mortality

	MMT		Heat-related RR		Cold-related RR	
Meta-variable	**Slope estimate [a] 95% CI**	**p-value**	**Slope estimate [a] 95% CI**	**p-value**	**Slope estimate [a] 95% CI**	**p-value**
Climate [b]						
Tmax	0.0019 (-0.0026 , 0.0064)	0.4096	-0.0002 (-0.0006 , 0.0002)	0.3278	-0.0001 (-0.0003 , 0.0001)	0.2552
Tmean	0.0073 (-0.0023 , 0.0168)	0.1372	-0.0014 (-0.0022 , -0.0006)	0.0003*	-0.0001 (-0.0005 , 0.0002)	0.4829
Tmin	0.0035 (-0.0003 , 0.0073)	0.0707	0 (-0.0003 , 0.0003)	0.8523	0.0002 (0 , 0.0003)	0.0362
RHmean	-0.0004 (-0.0037 , 0.0029)	0.8096	0 (-0.0003 , 0.0003)	0.9343	0.0002 (0.0001 , 0.0003)	0.0076*
Demographic [c]						
% ≤ 4 years	-7.4769 (-12.7499 , -2.2039)	0.0055*	-1.0545 (-1.3764 , -0.7325)	0.0000*	0.0179 (-0.1535 , 0.1893)	0.8375
% 5–9 years	-2.8498 (-7.5558 , 1.8562)	0.2351	-0.4513 (-0.7767 , -0.1259)	0.0066*	-0.3399 (-0.4932 , -0.1865)	0.0000*
% ≥ 65 years	-2.2754 (-6.6394 , 2.0887)	0.3066	-0.2466 (-0.57 , 0.0768)	0.1350	0.3206 (0.1099 , 0.5313)	0.0029*
Socio-economic [d]						
Savings	0.125 (0.0757 , 0.1744)	0.0000*	0.0007 (-0.0026 , 0.004)	0.6675	-0.0034 (-0.006 , -0.0008)	0.0103
EPI	2.3067 (0.7698 , 3.8436)	0.0036*	-0.0115 (-0.0332 , 0.0102)	0.3002	-0.0694 (-0.101 , -0.0378)	0.0000*
CPI	-0.0002 (-0.0049 , 0.0045)	0.9308	-0.0003 (-0.0007 , 0)	0.0373*	-0.0001 (-0.0002 , 0.0001)	0.4256
Air conditioning [e]						
AC	-0.0007 (-0.0026 , 0.0012)	0.4715	0.0001 (0 , 0.0002)	0.1937	0 (-0.0001 , 0)	0.1369

[a] Change in each outcome [MMT in °C, heat- and cold-related mortality ln(RR)] per 1-unit increase in each meta-variable. Each meta-variable is scaled such that the slope estimate is not a value very close to zero.

[b] Climate variables for 1972–2012 (annual values, N = 41): Tmax (maximum daily mean temperature), Tmean (average daily mean temperature), Tmin (minimum daily mean temperature) and RHmean (average daily mean relative humidity)

[c] Demographic variables for 1972–2012 (annual values, N = 41): Percent of population ≤ 4, 5–9, and ≥ 65 years of age.

[d] Socio-economic variables: Savings (annual average savings per household with two or more persons, available every 5 years from 1974–2009, N = 8), EPI (economic power index, a measure of financial strength of a local government, higher value represents more strength, 2003-2010, N =8), CPI (consumer price index, measure of the cost of goods and services by household, 1972-2012, N = 41)

[e] Air conditioning prevalence for households with two or more persons, 1972-2009 (N = 38)

* p-value<0.01

Table S4. Association between each aspect (MMT, heat- and cold-related mortality risks) and each meta-variable in male mortality

	MMT		Heat-related RR		Cold-related RR	
Meta-variable	**Slope estimate [a] 95% CI**	**p-value**	**Slope estimate [a] 95% CI**	**p-value**	**Slope estimate [a] 95% CI**	**p-value**
Climate [b]						
Tmax	-0.0035 (-0.007 , 0.0001)	0.0548	-0.0002 (-0.0004 , 0.0001)	0.1717	0 (-0.0001 , 0.0002)	0.7145
Tmean	0.0054 (-0.0021 , 0.0129)	0.1603	-0.0007 (-0.0011 , -0.0002)	0.0031*	0 (-0.0004 , 0.0004)	0.9864
Tmin	0.0036 (0.0007 , 0.0066)	0.0166	0.0001 (-0.0001 , 0.0002)	0.5426	0.0002 (0.0001 , 0.0004)	0.0073*
RHmean	-0.0013 (-0.0038 , 0.0012)	0.3008	0 (-0.0001 , 0.0002)	0.5678	-0.0001 (-0.0003 , 0)	0.0801
Demographic [c]						
% ≤ 4 years	-5.7032 (-9.9732 , -1.4332)	0.0089*	-0.463 (-0.6654 , -0.2607)	0.0000*	0.6795 (0.5013 , 0.8577)	0.0000*
% 5–9 years	-5.6055 (-9.5031 , -1.7079)	0.0048*	-0.0604 (-0.2548 , 0.1341)	0.5427	0.0367 (-0.1264 , 0.1998)	0.6590
% ≥ 65 years	7.6721 (4.5135 , 10.8308)	0.0000*	-0.2366 (-0.4799 , 0.0067)	0.0567	0.3123 (0.1052 , 0.5195)	0.0031*
Socio-economic [d]						
Savings	0.0049 (-0.02 , 0.0297)	0.6991	0.0002 (-0.0019 , 0.0022)	0.8851	0 (-0.0018 , 0.0019)	0.9876
EPI	-0.432 (-1.2481 , 3.8413)	0.3018	-0.0163 (-0.0328 , 0.0002)	0.0543	0.0017 (-0.0218 , 0.0253)	0.8862
CPI	0.0014 (-0.0022 , 0.0051)	0.4378	-0.0001 (-0.0003 , 0.0001)	0.2797	0.0006 (0.0005 , 0.0008)	0.0000*
Air conditioning [e]						
AC	0.0005 (-0.0004 , 0.0015)	0.2855	0.0001 (0 , 0.0001)	0.1428	-0.0001 (-0.0001 , 0)	0.0727

[a] Change in each outcome [MMT in °C, heat- and cold-related mortality ln(RR)] per 1-unit increase in each meta-variable. Each meta-variable is scaled such that the slope estimate is not a value very close to zero.

[b] Climate variables for 1972–2012 (annual values, N = 41): Tmax (maximum daily mean temperature), Tmean (average daily mean temperature), Tmin (minimum daily mean temperature) and RHmean (average daily mean relative humidity)

[c] Demographic variables for 1972–2012 (annual values, N = 41): Percent of population ≤ 4, 5–9, and ≥ 65 years of age.

[d] Socio-economic variables: Savings (annual average savings per household with two or more persons, available every 5 years from 1974–2009, N = 8), EPI (economic power index, a measure of financial strength of a local government, higher value represents more strength, 2003-2010, N =8), CPI (consumer price index, measure of the cost of goods and services by household, 1972-2012, N = 41)

[e] Air conditioning prevalence for households with two or more persons, 1972-2009 (N = 38)

* p-value<0.01

Figure S1. Map of the 47 prefectures in Japan. Blue and red indicate the eastern and western prefectures, respectively.

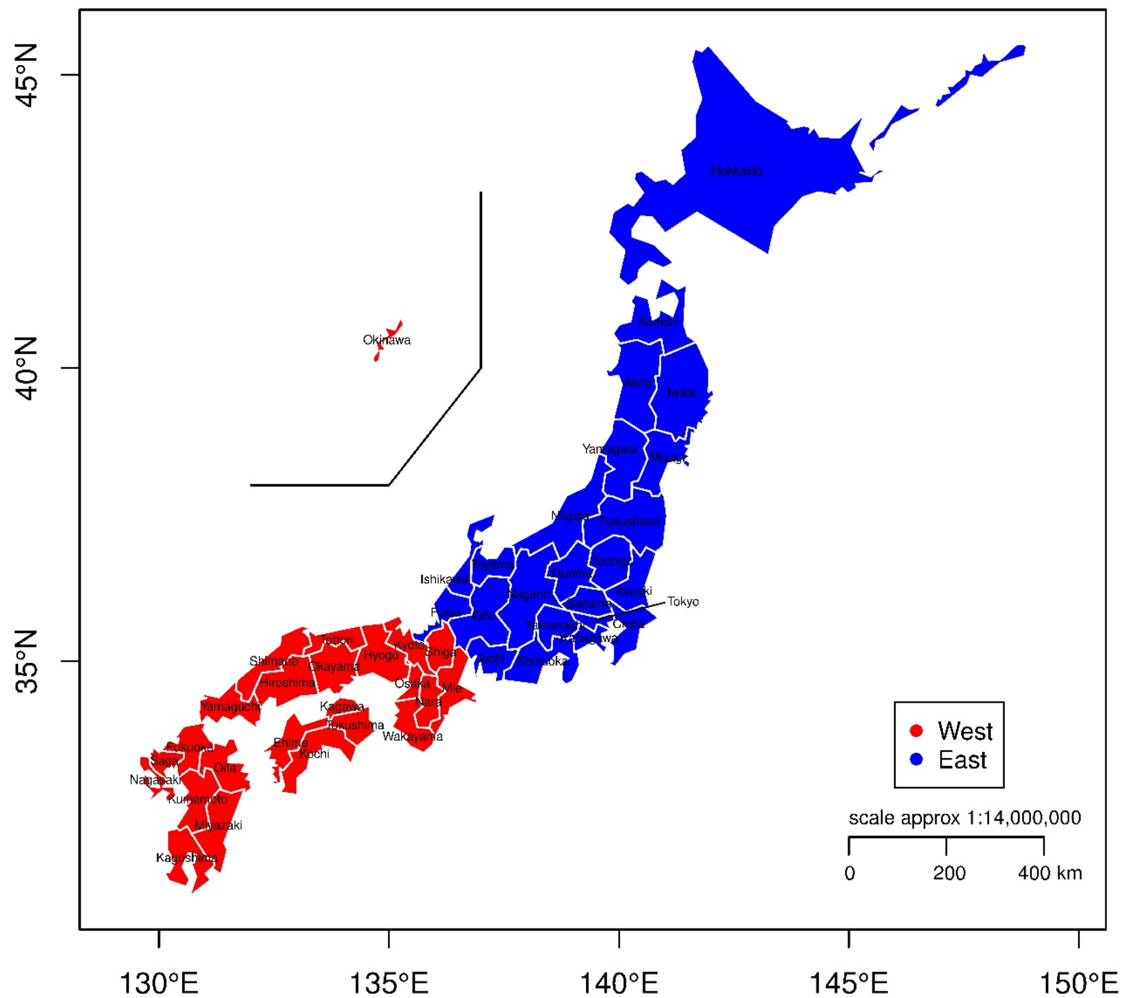


Figure S2. Time-series plot for each of the prefecture-specific meta-variables. Blue and red indicate the eastern and western prefectures, respectively.

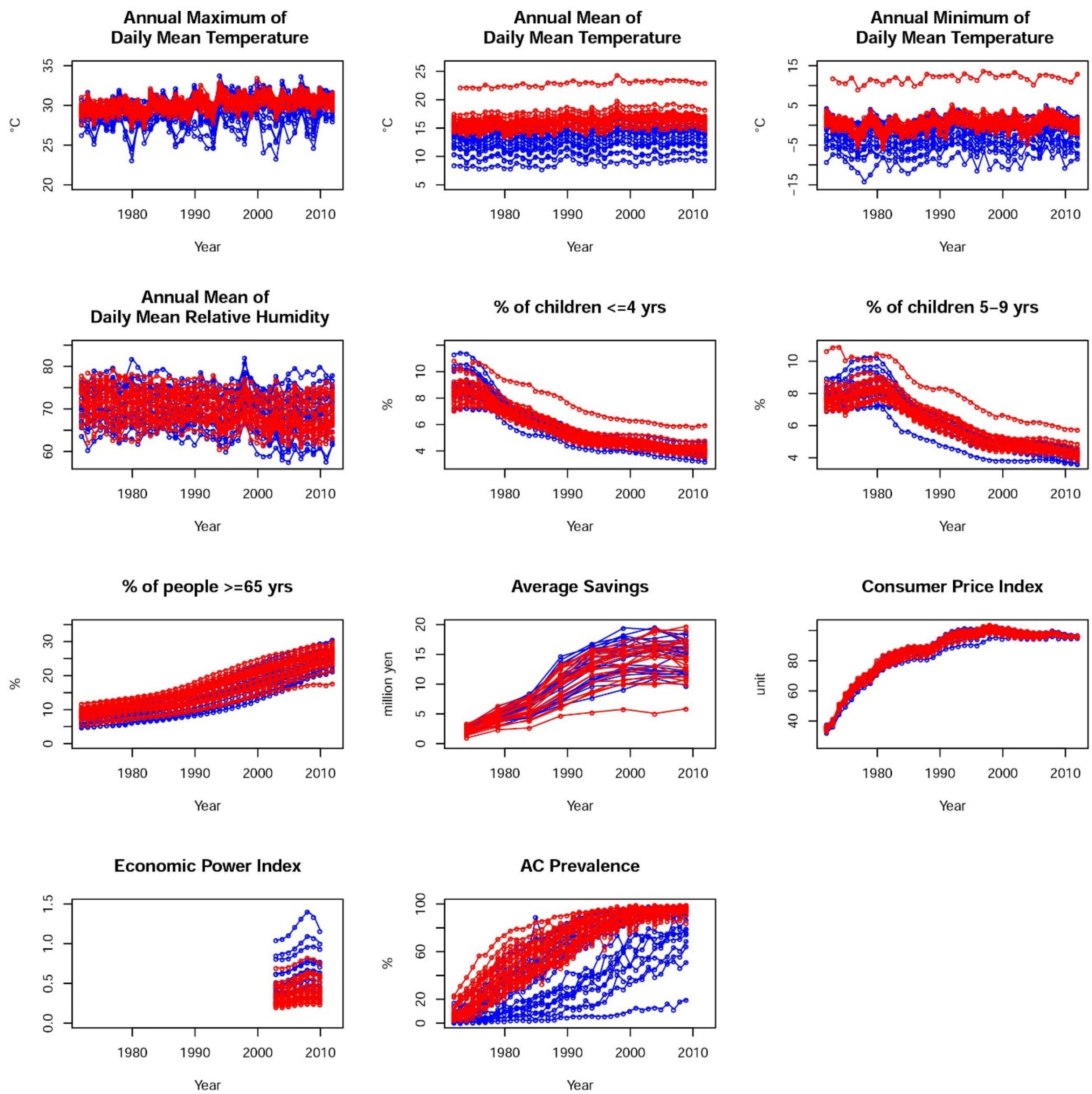
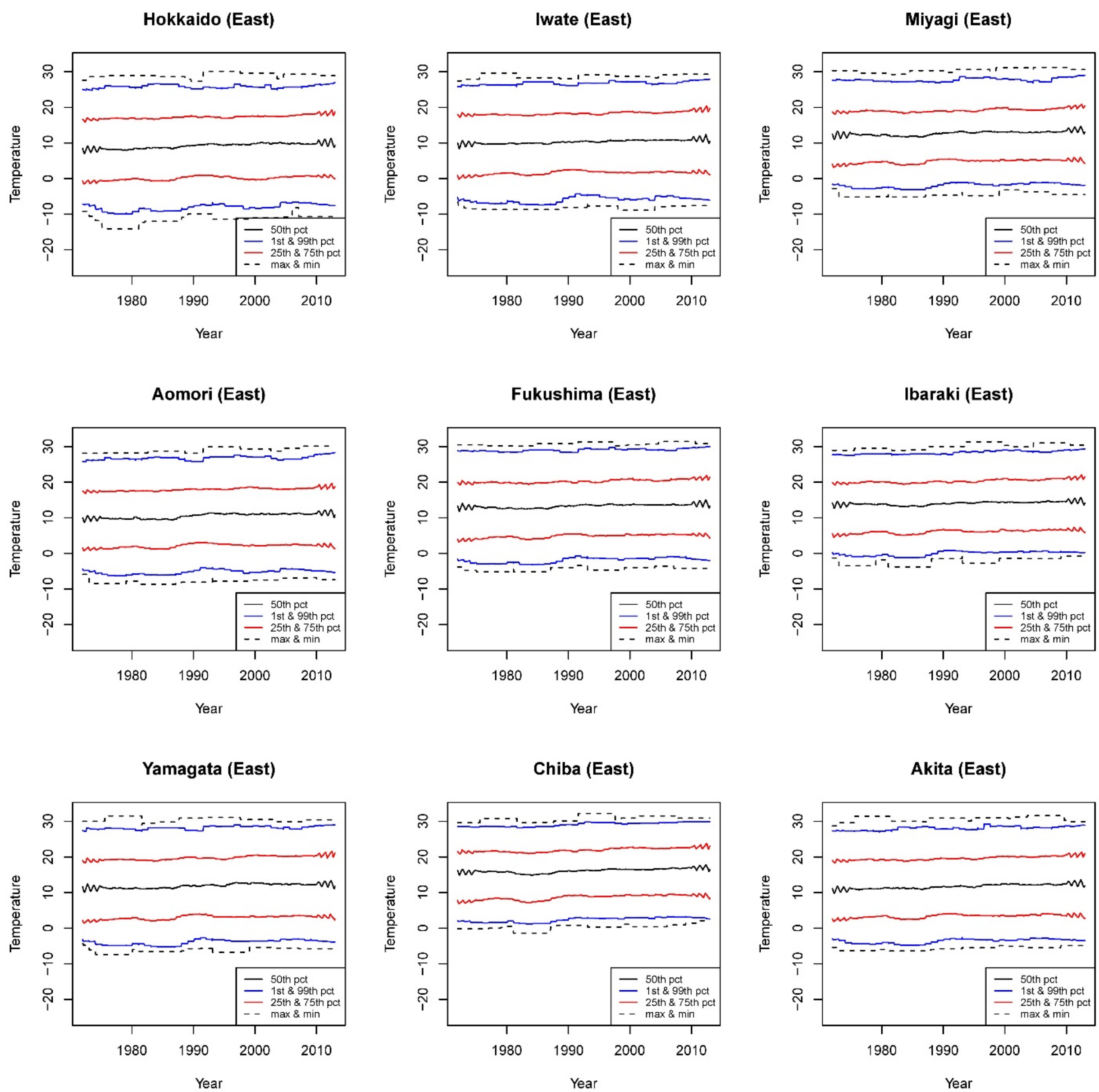
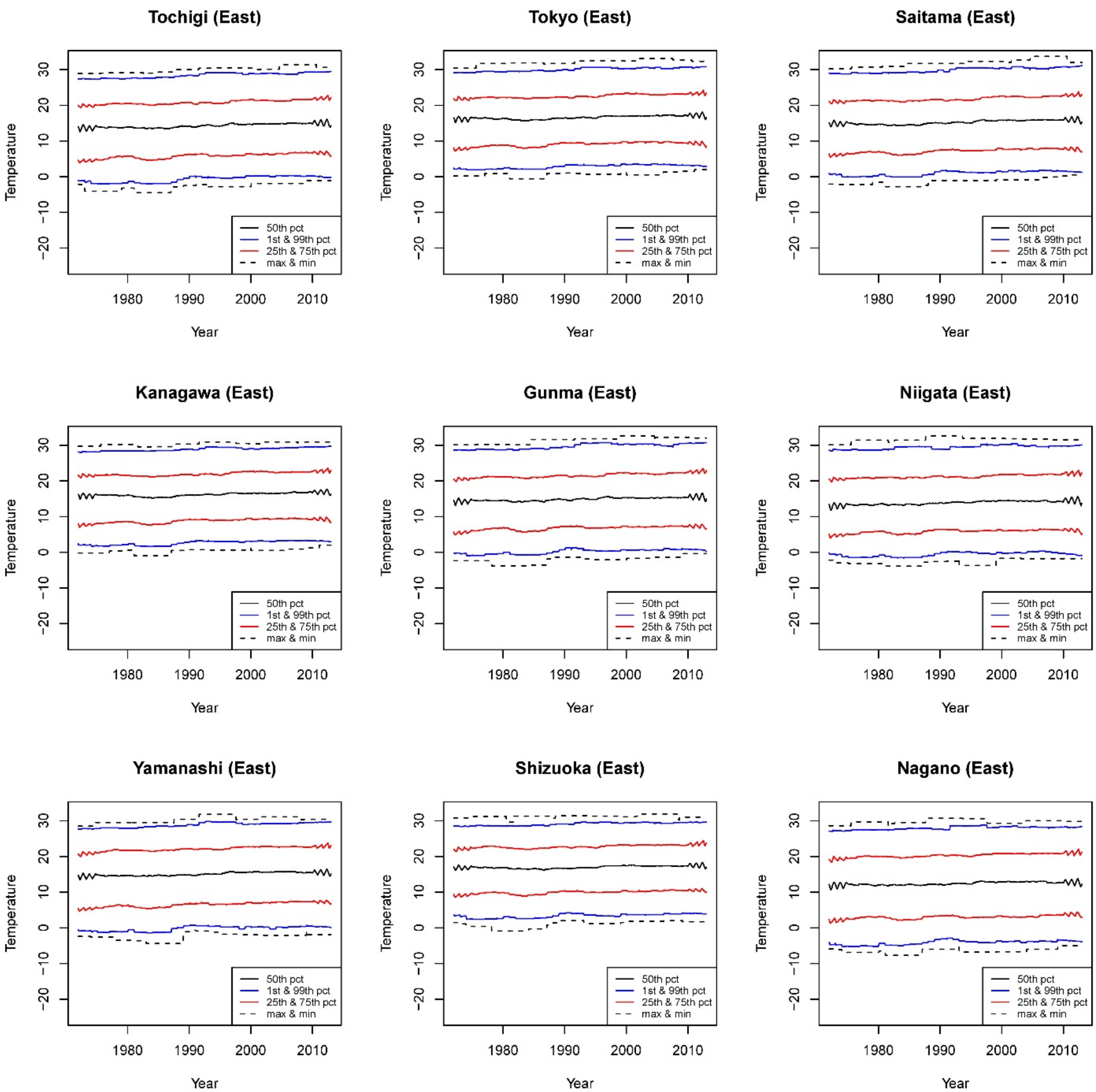


Figure S3. Prefecture-specific time-varying temperature distribution (minimum, 1st, 25th, 50th, 75th, 99th percentiles, and maximum). At each time point, a temperature distribution was defined using the daily mean temperatures for the 6-year moving period with the specific time point as a center.

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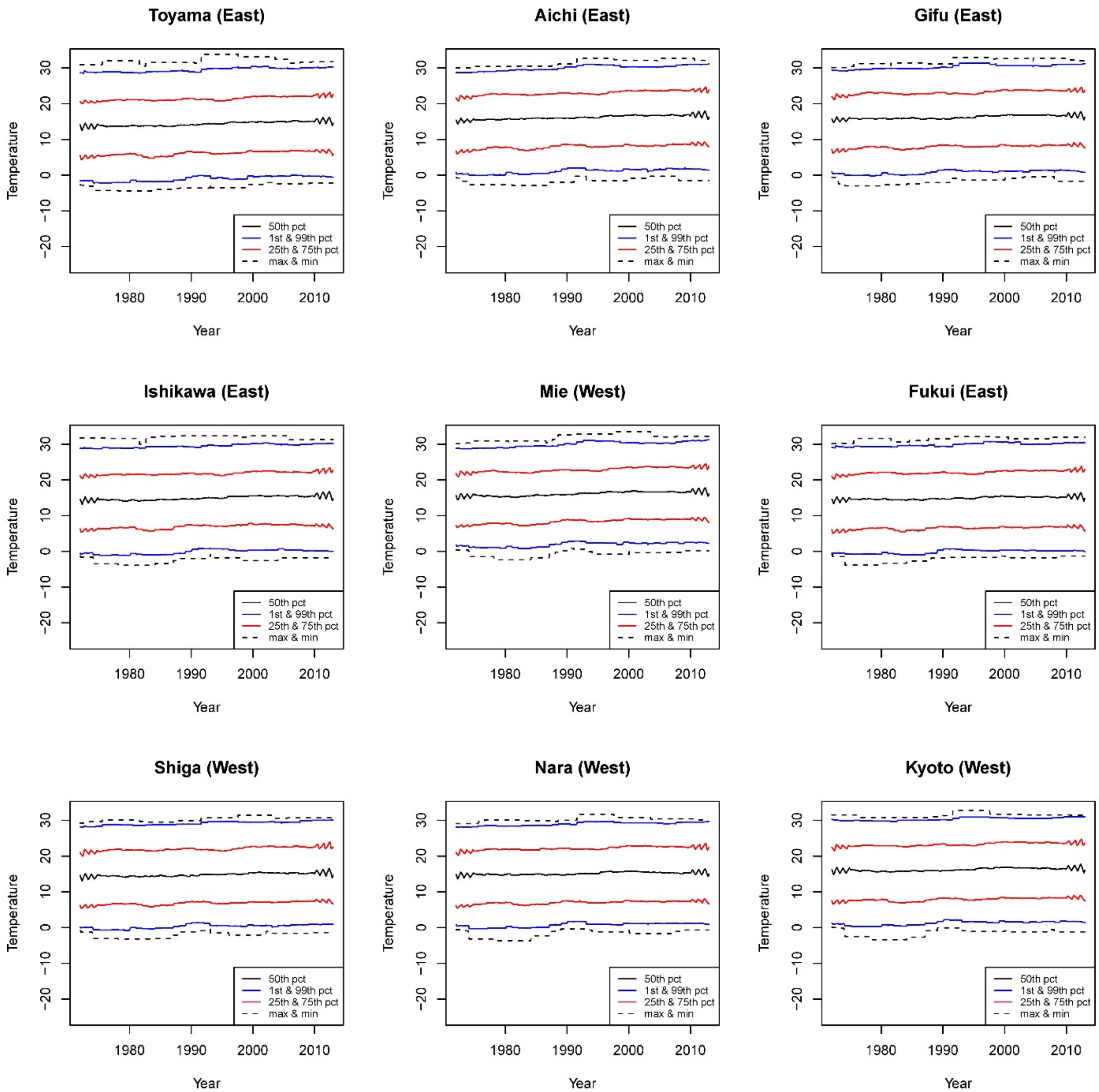
Tokyo (East)
Saitama (East)
Kanagawa (East)
Gunma (East)
Niigata (East)
Yamanashi (East)
Shizuoka (East)
Nagano (East)
Temperature
Year
30
20
10
0
−10
−20
1980
1990
2000
2010
50th pct
1st & 99th pct
25th & 75th pct
max & min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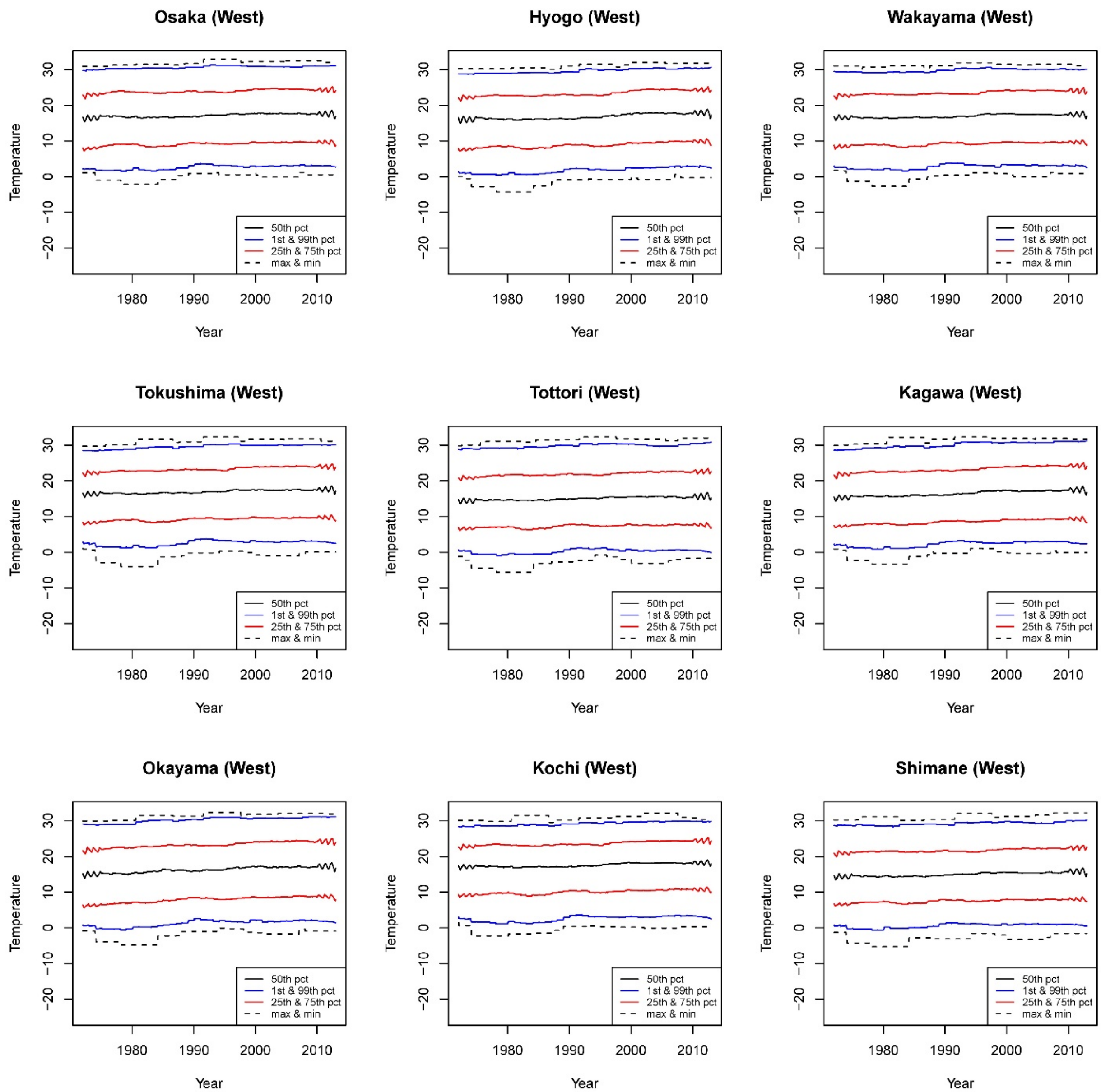
Gifu (East)
Ishikawa (East)
Mie (West)
Fukui (East)
Shiga (West)
Nara (West)
Kyoto (West)
Temperature
Year
-20
-10
0
10
20
30
1980
1990
2000
2010
50th pct
1st & 99th pct
25th & 75th pct
max & min



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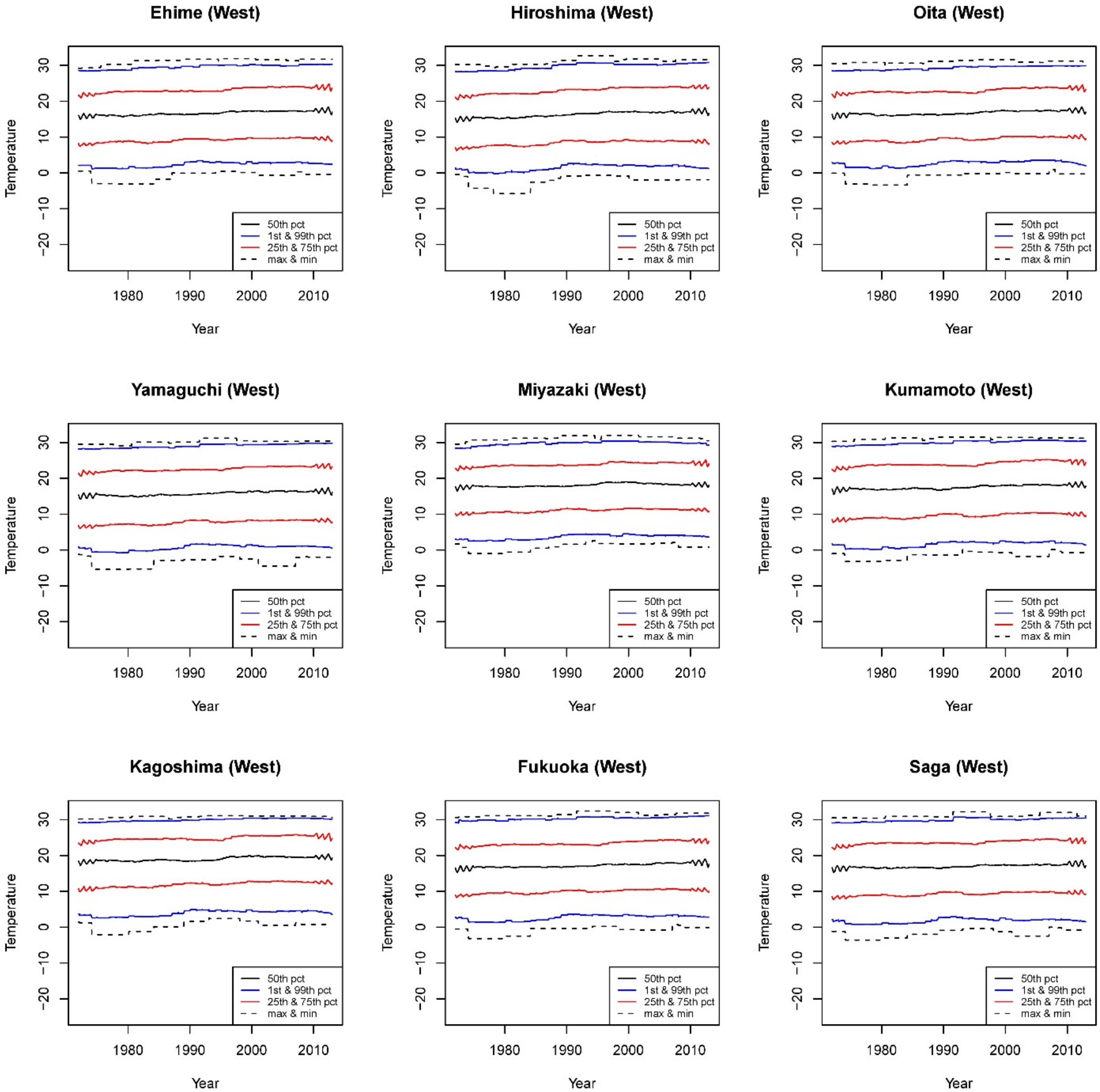
Hyogo (West)
Wakayama (West)
Tokushima (West)
Tottori (West)
Kagawa (West)
Okayama (West)
Kochi (West)
Shimane (West)
Temperature
Year
50th pct
1st & 99th pct
25th & 75th pct
max & min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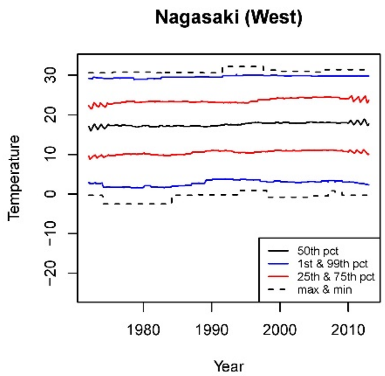
Yamaguchi (West)
Miyazaki (West)
Kumamoto (West)
Kagoshima (West)
Fukuoka (West)
Saga (West)
Temperature
Year
50th pct
1st & 99th pct
25th & 75th pct
max & min
30
20
10
0
−10
−20
1980
1990
2000
2010


Nagasaki (West)
Temperature
Year
50th pct
1st & 99th pct
25th & 75th pct
max & min

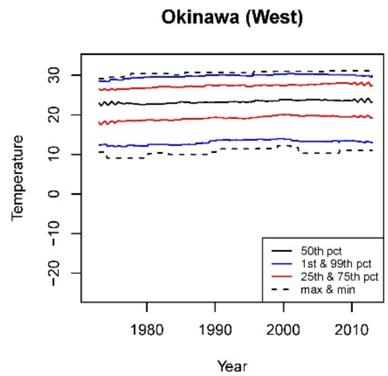

Okinawa (West)
Temperature
Year
50th pct
1st & 99th pct
25th & 75th pct
max & min

Figure S4. Region-specific time-varying minimum mortality temperature (MMT) together with the time-varying minimum mortality temperature percentile (MMTP) (top), time-varying heat-related mortality risk (middle), and time-varying cold-related mortality risk (bottom). Black solid and dashed lines indicate the point estimate of the MMT and 95% point-wise confidence intervals, respectively. Blue line in the top panels indicates the MMTP.

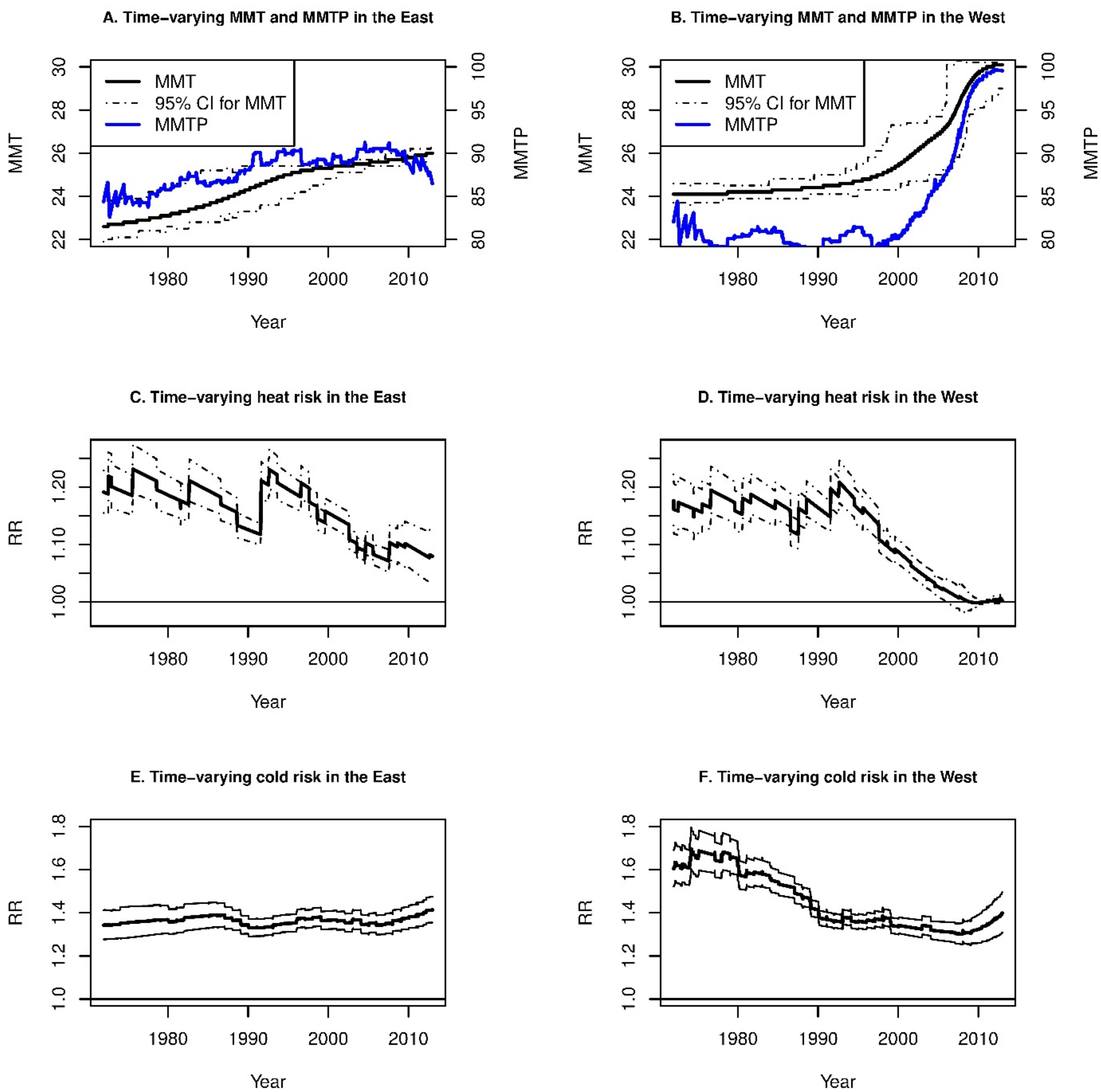
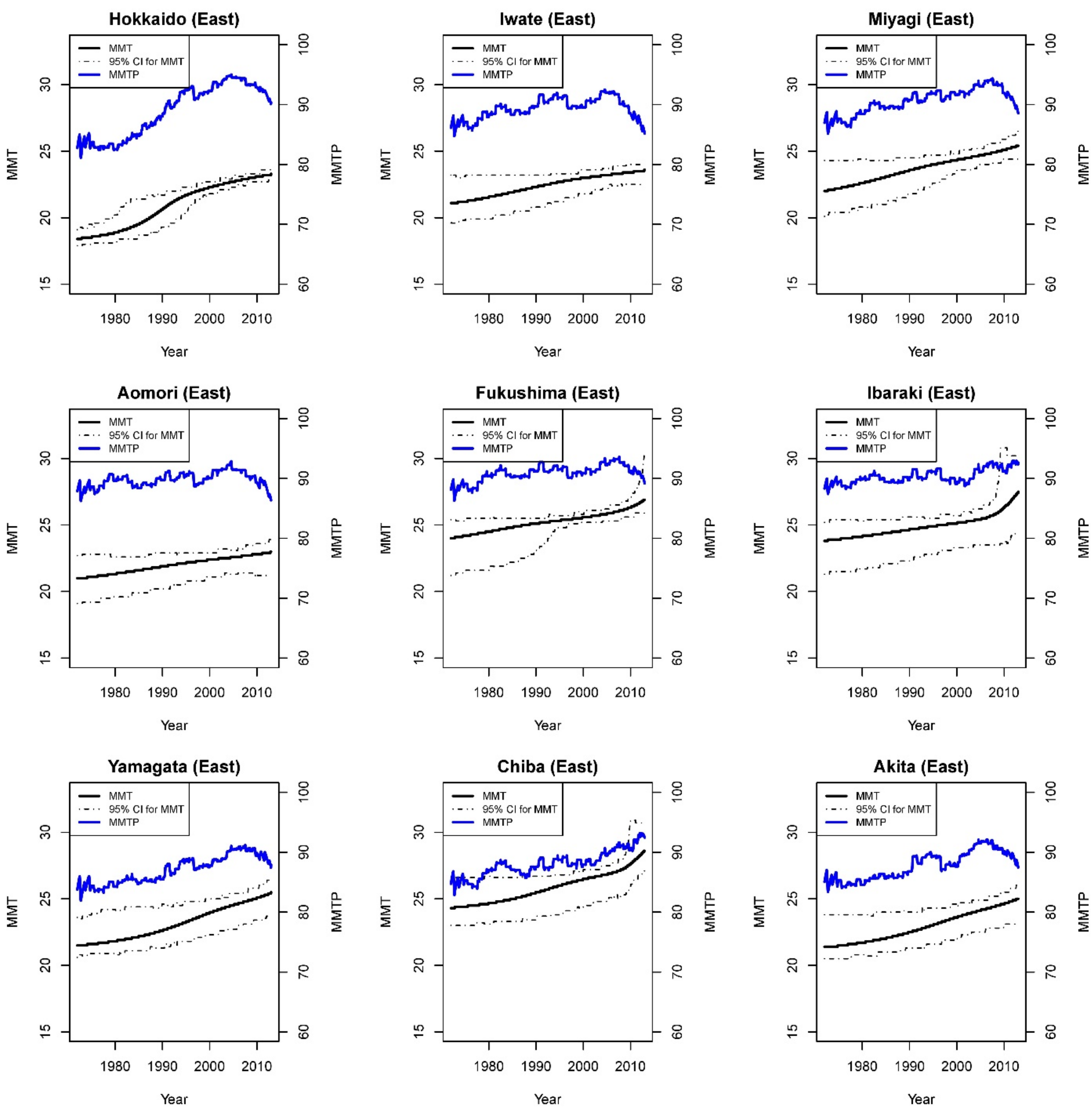
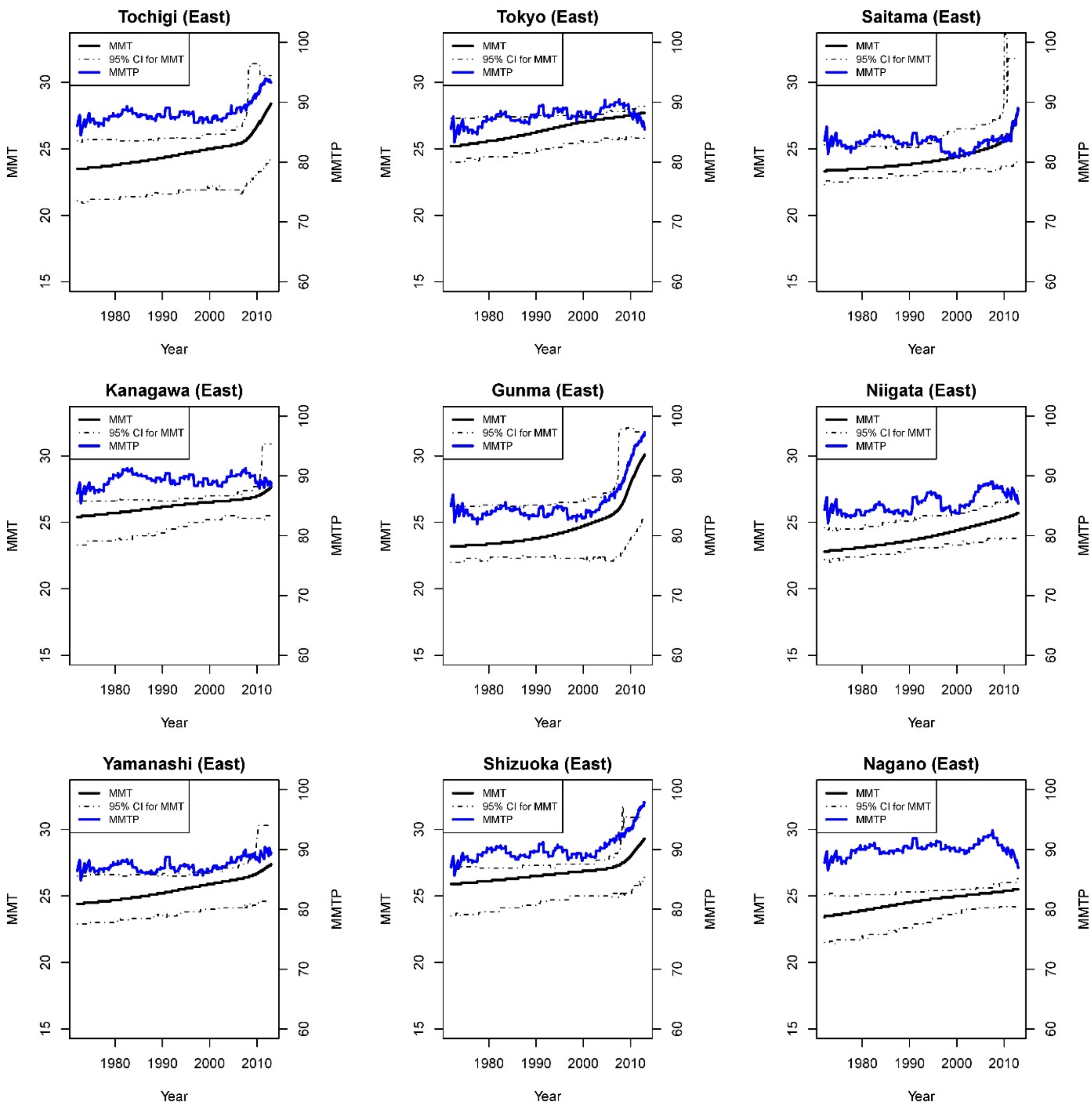


Figure S5. Prefecture-specific time-varying minimum mortality temperature (MMT) and minimum mortality temperature percentile (MMTP). Black solid and dashed lines indicate the point estimate of the MMT and 95% point-wise confidence intervals, respectively. Blue line indicates the MMTP.

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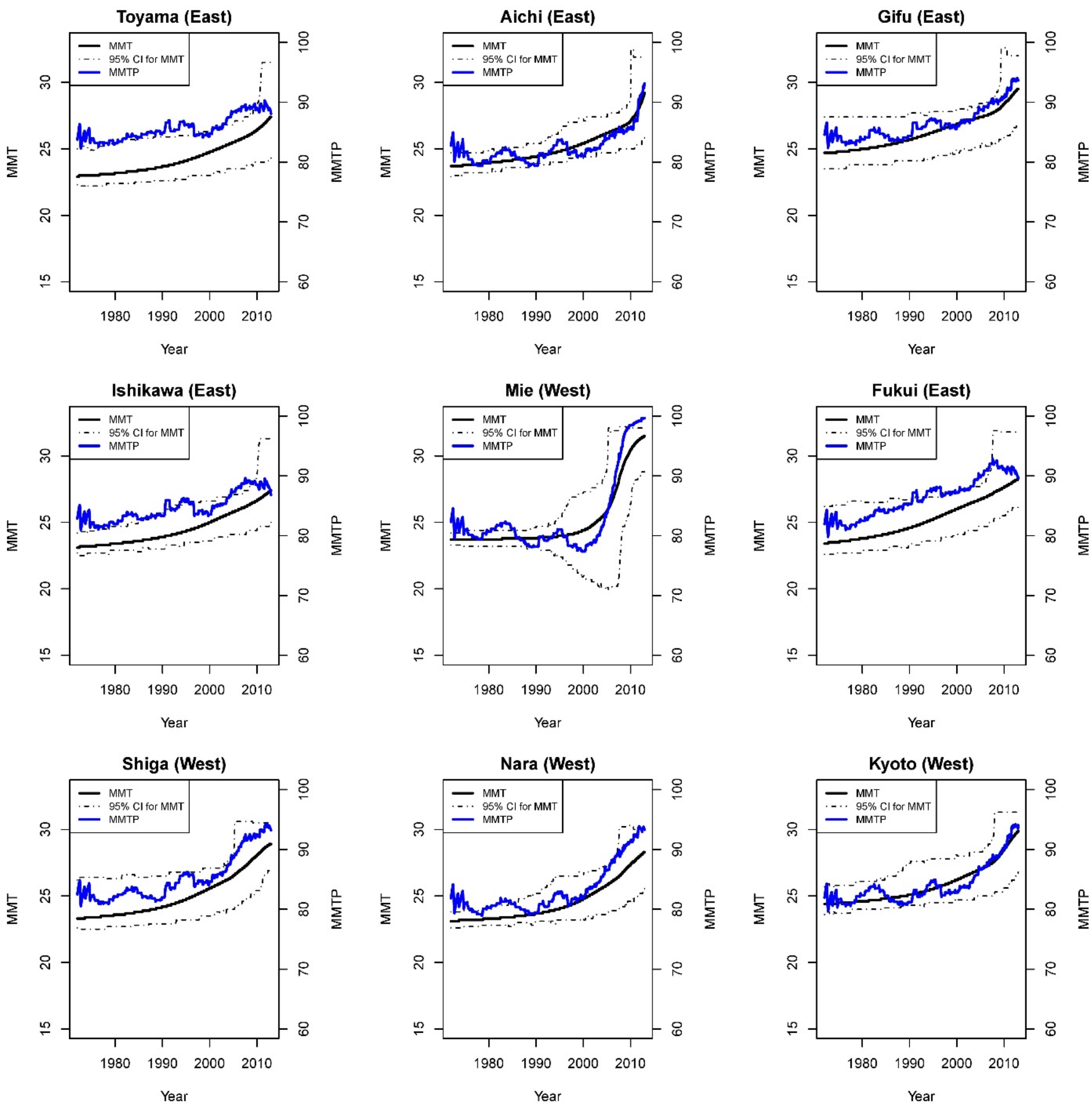
Tokyo (East)
Saitama (East)
Kanagawa (East)
Gunma (East)
Niigata (East)
Yamanashi (East)
Shizuoka (East)
Nagano (East)
MMT
95% CI for MMT
MMTP
Year
1980
1990
2000
2010
15
20
25
30
60
70
80
90
100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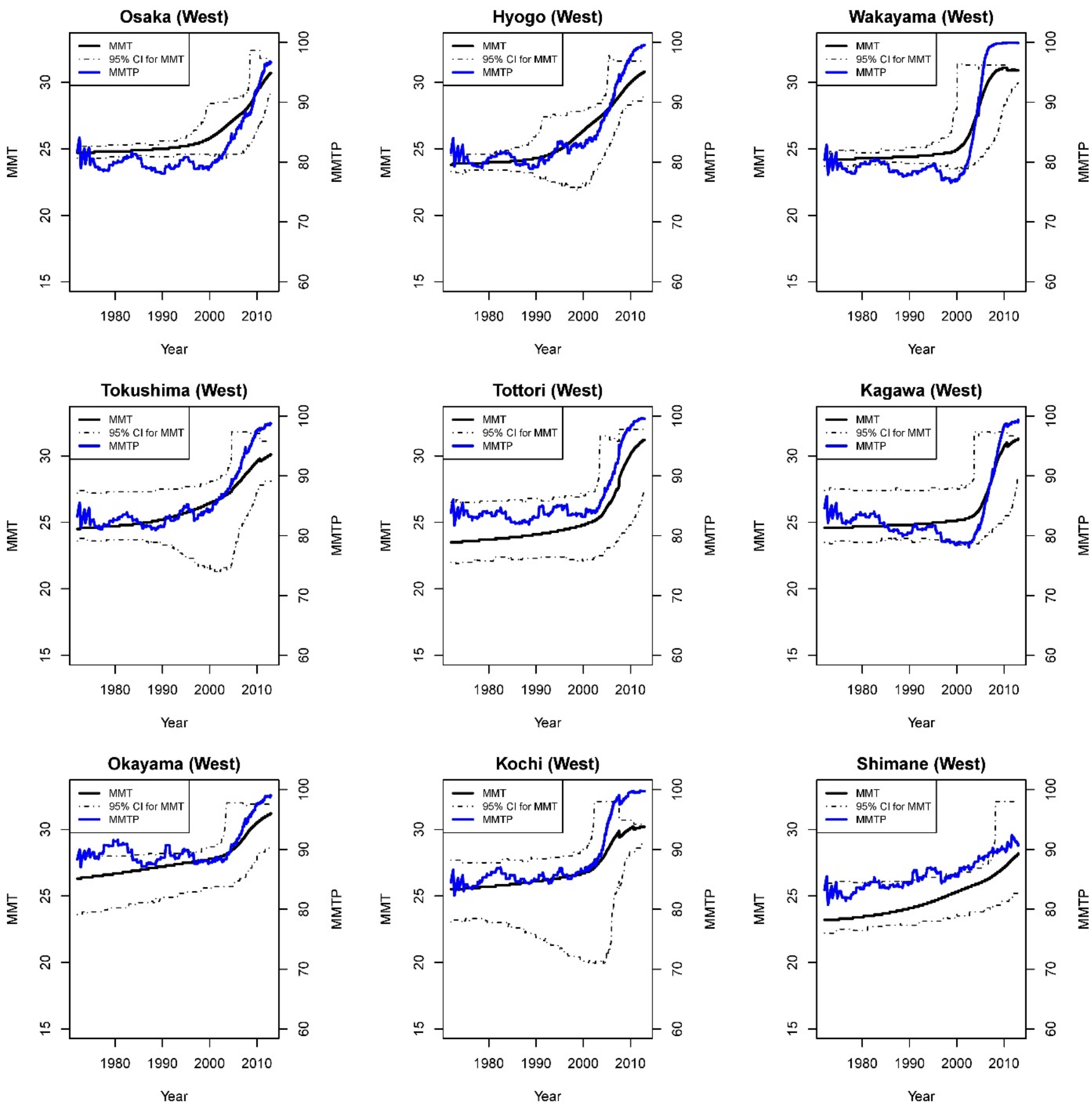
Fukui (East)
Shiga (West)
Nara (West)
Kyoto (West)
MMT
95% CI for MMT
MMTP
Year
1980
1990
2000
2010
15
20
25
30
60
70
80
90
100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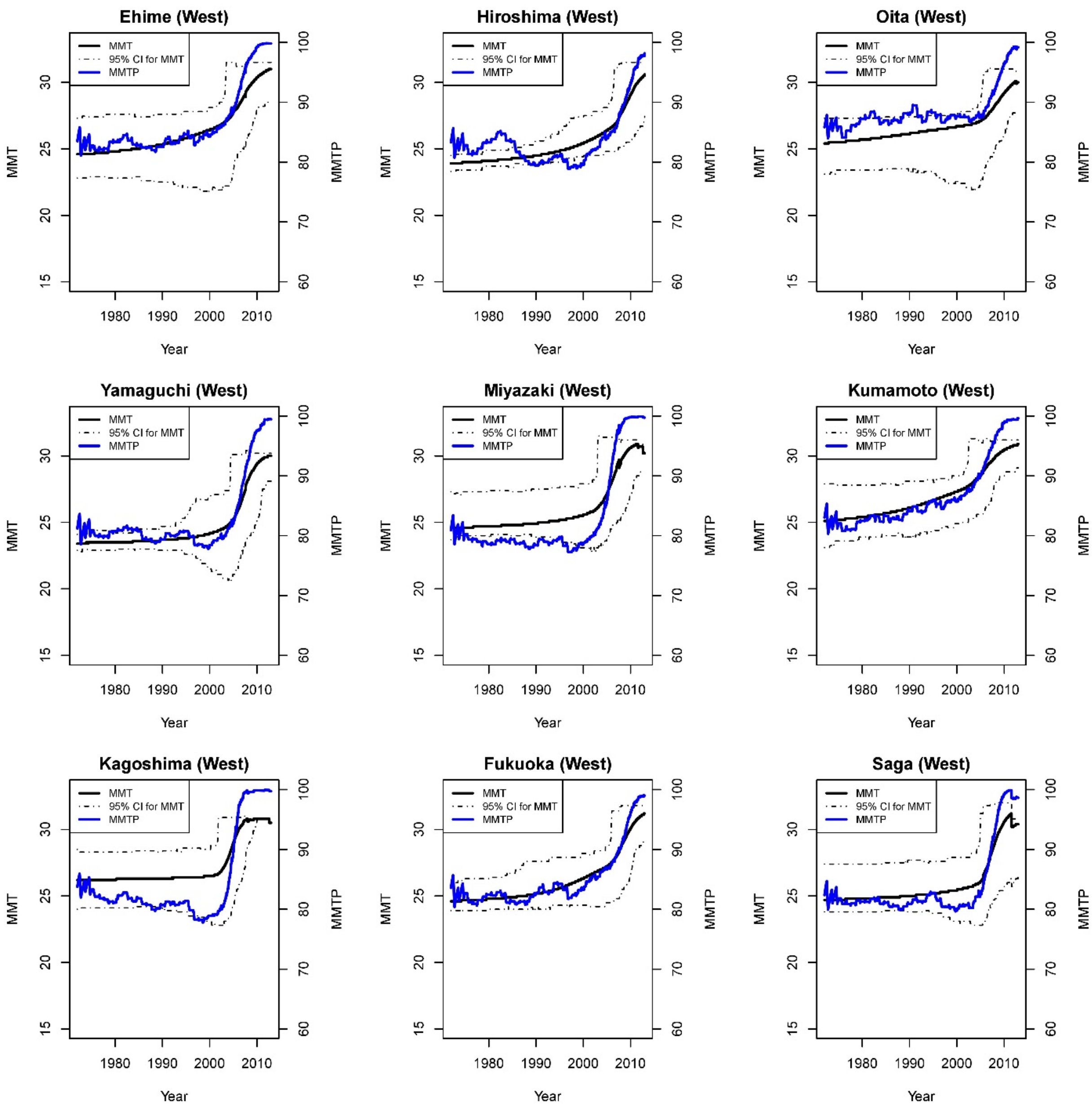
Tottori (West)
Kagawa (West)
Okayama (West)
Kochi (West)
Shimane (West)
MMT
95% CI for MMT
MMTP
Year
1980
1990
2000
2010
15
20
25
30
60
70
80
90
100



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Oita (West)
Yamaguchi (West)
Miyazaki (West)
Kumamoto (West)
Kagoshima (West)
Fukuoka (West)
Saga (West)
MMT
95% CI for MMT
MMTP
Year
1980
1990
2000
2010
15
20
25
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60
70
80
90
100

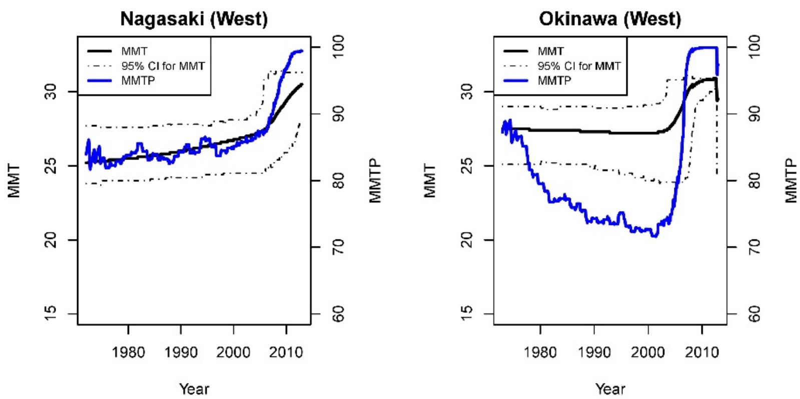
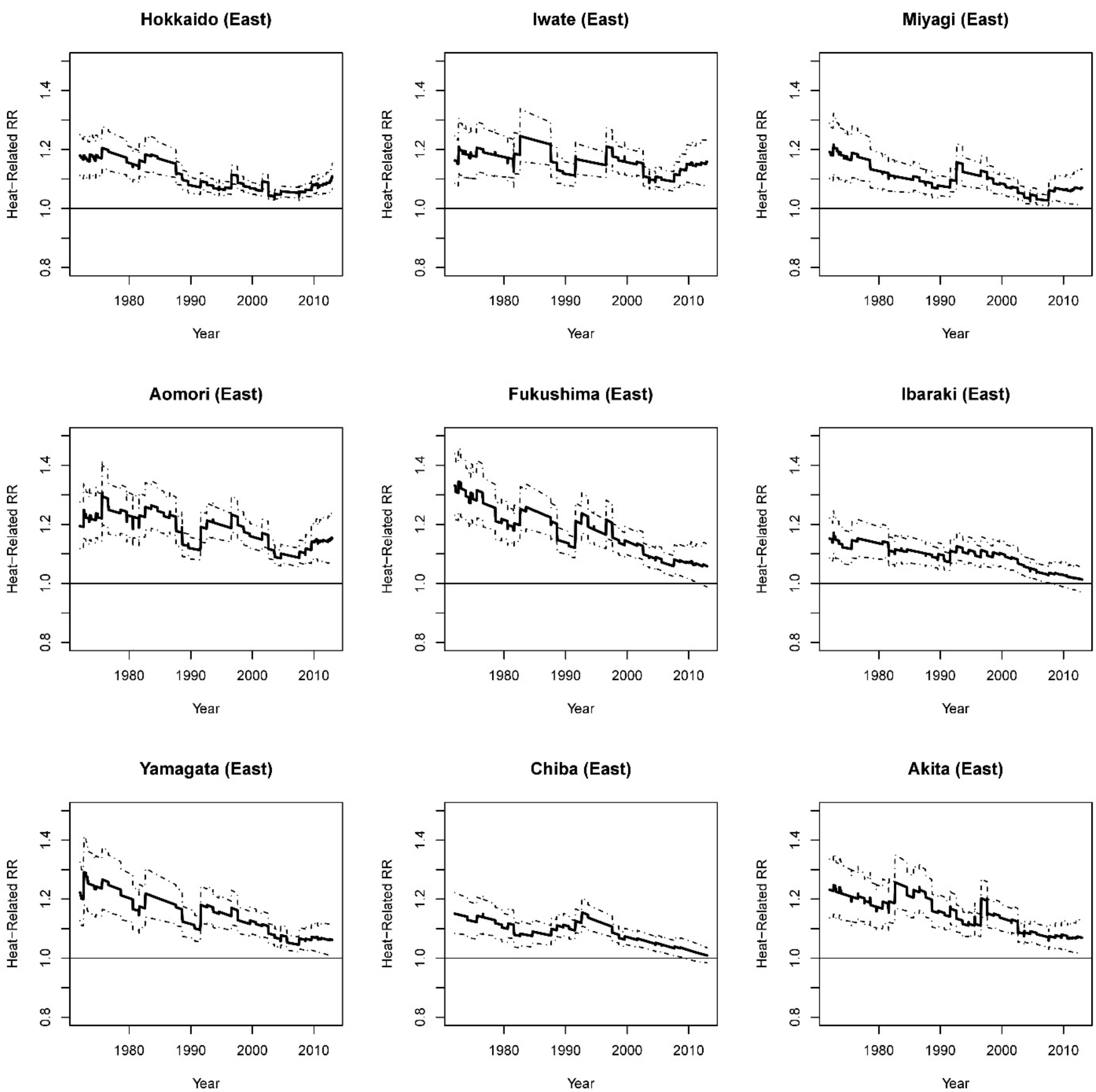
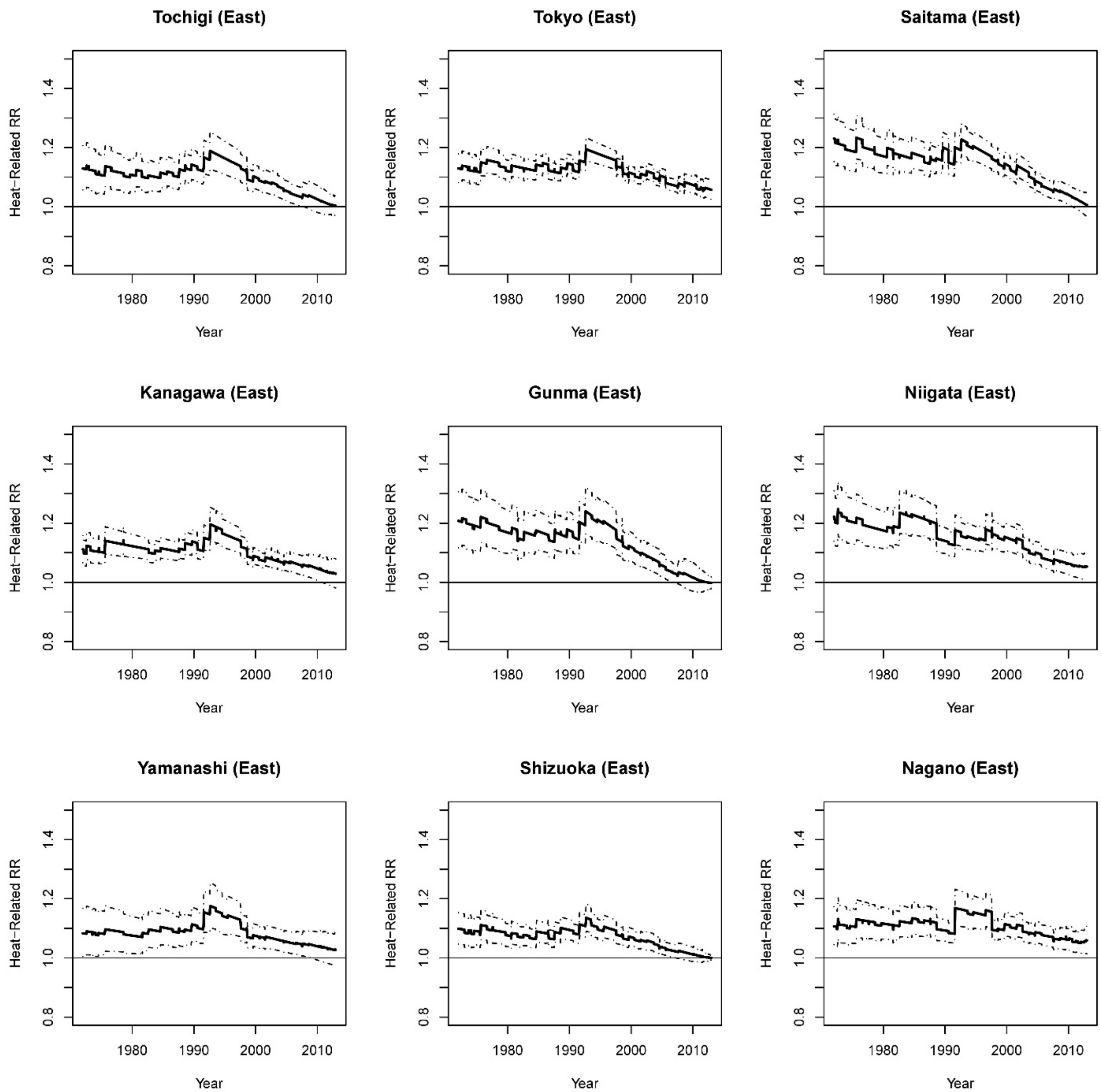

Nagasaki (West)
MMT
95% CI for MMT
MMTP
MMT
MMTP
Year
Okinawa (West)
MMT
95% CI for MMT
MMTP
MMT
MMTP
Year

Figure S6. Prefecture-specific time-varying heat-related mortality risk. The heat-related risk was defined as the relative risk comparing the time-varying minimum mortality temperature (MMT) and the time-varying 99th temperature percentile. Black solid and dashed lines indicate the point estimate of the heat risk and 95% point-wise confidence intervals, respectively.

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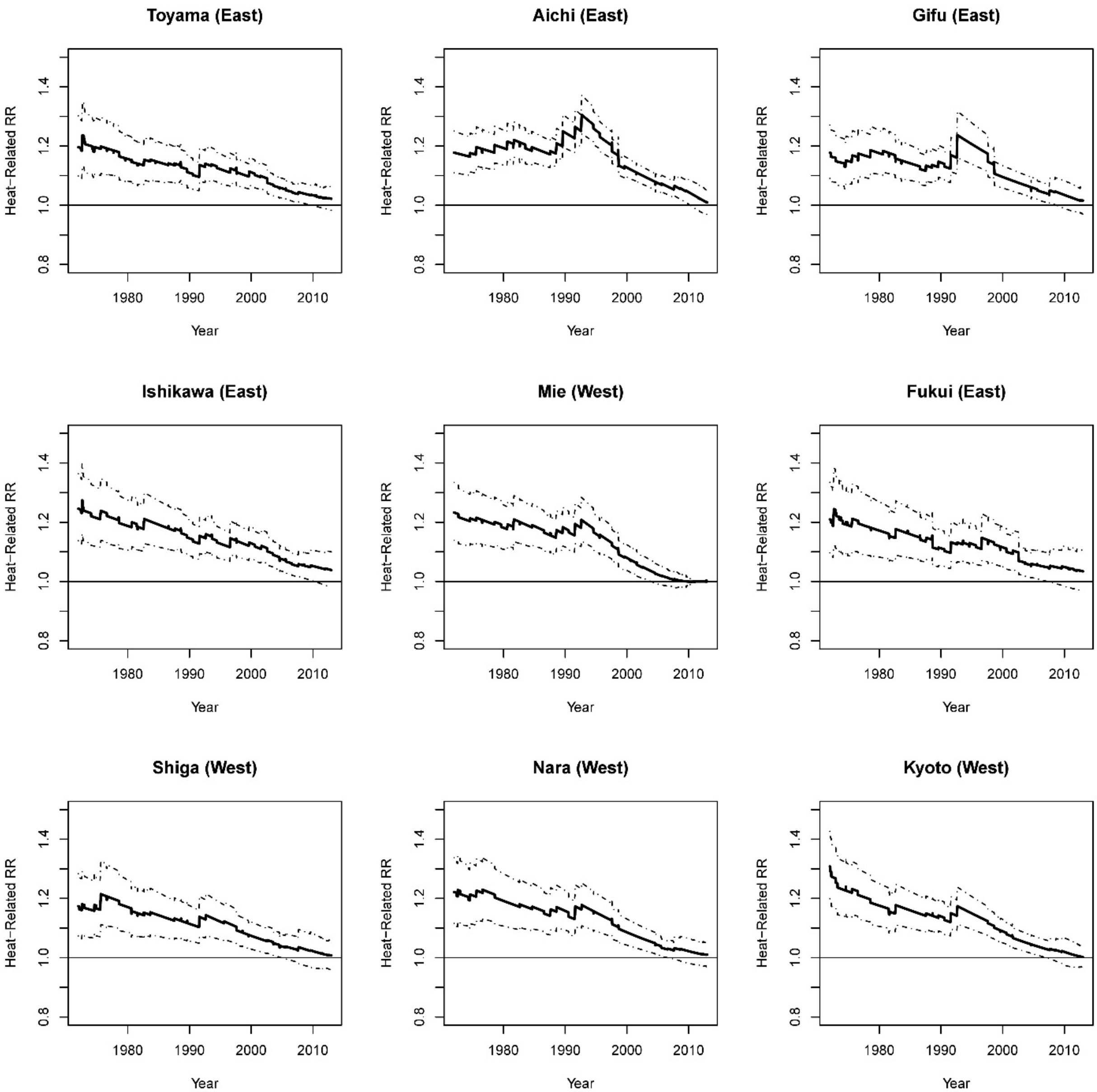
Saitama (East)
Kanagawa (East)
Gunma (East)
Niigata (East)
Yamanashi (East)
Shizuoka (East)
Nagano (East)
Heat−Related RR
Year
0.8
1.0
1.2
1.4
1980
1990
2000
2010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Fukui (East)
Shiga (West)
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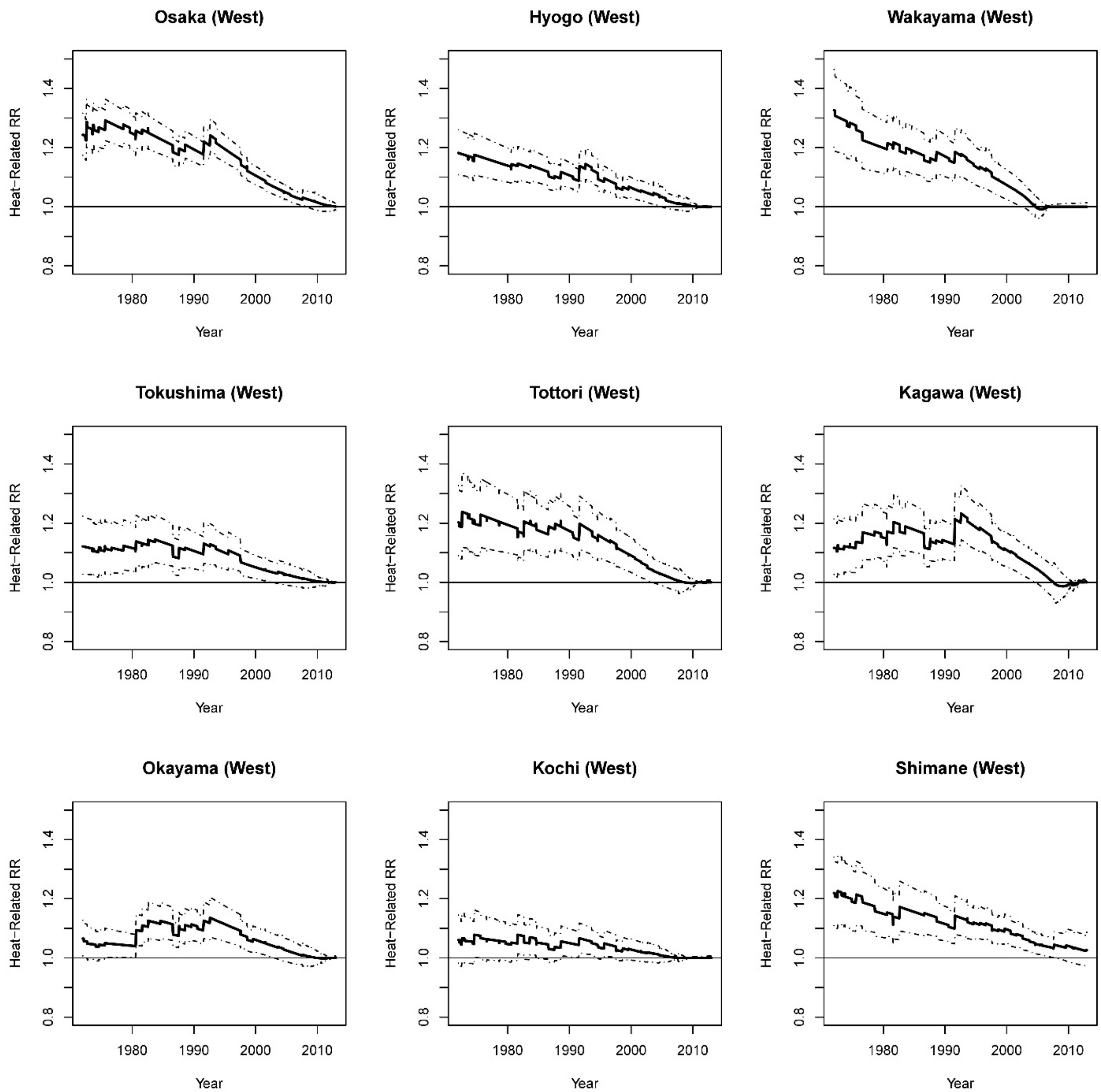
Kyoto (West)
Heat−Related RR
Year
0.8
1.0
1.2
1.4
1980
1990
2000
2010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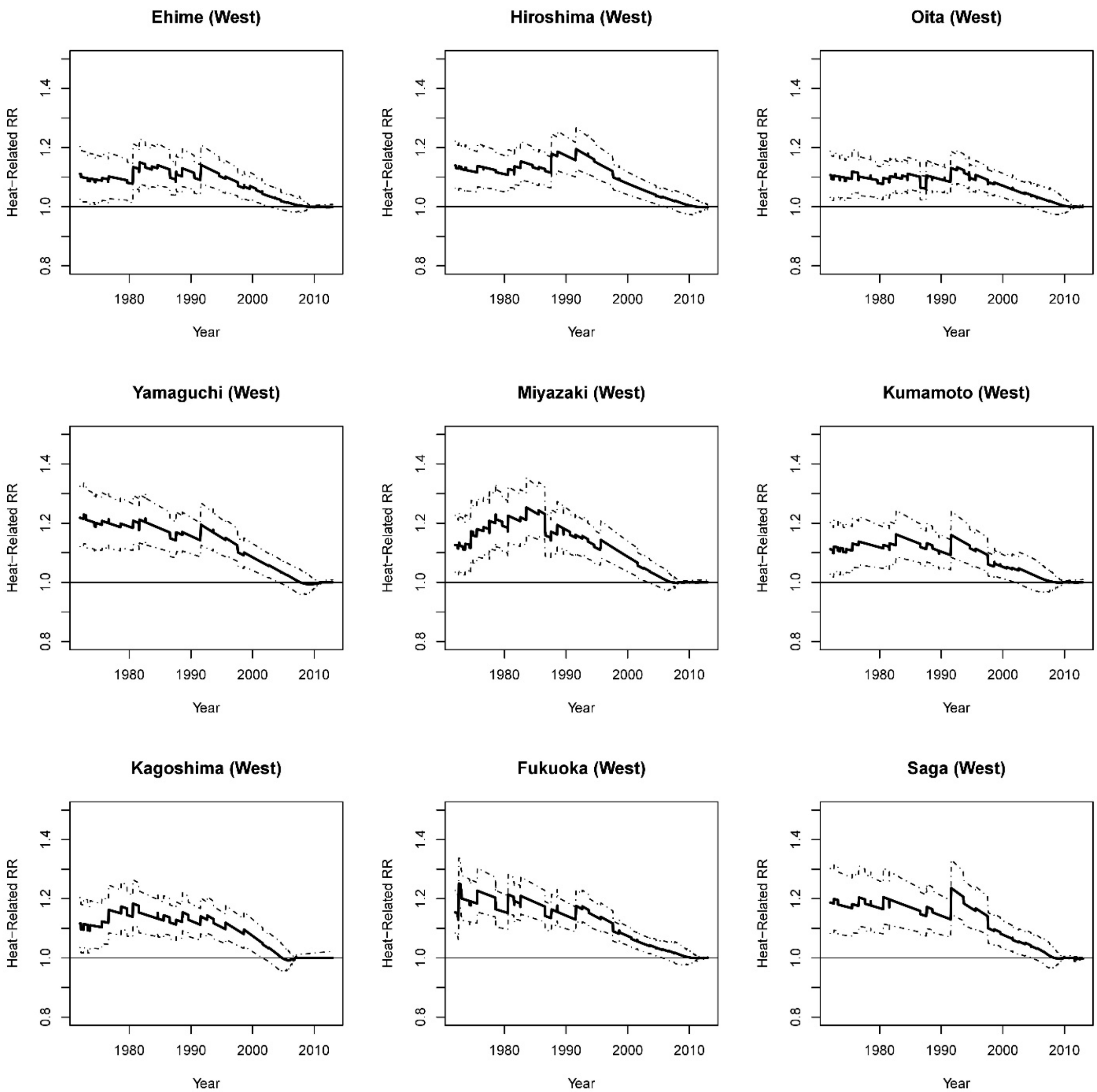
Wakayama (West)
Tokushima (West)
Tottori (West)
Kagawa (West)
Okayama (West)
Kochi (West)
Shimane (West)
Heat−Related RR
Year
0.8
1.0
1.2
1.4
1980
1990
2000
2010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Oita (West)
Yamaguchi (West)
Miyazaki (West)
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Kagoshima (West)
Fukuoka (West)
Saga (West)
Heat−Related RR
0.8
1.0
1.2
1.4
1980
1990
2000
2010
Year

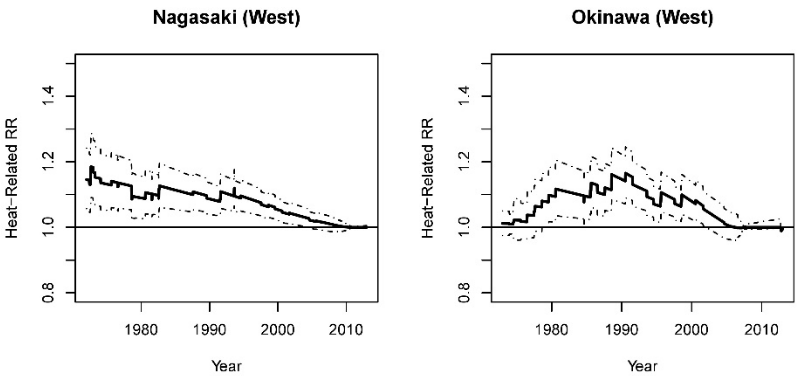
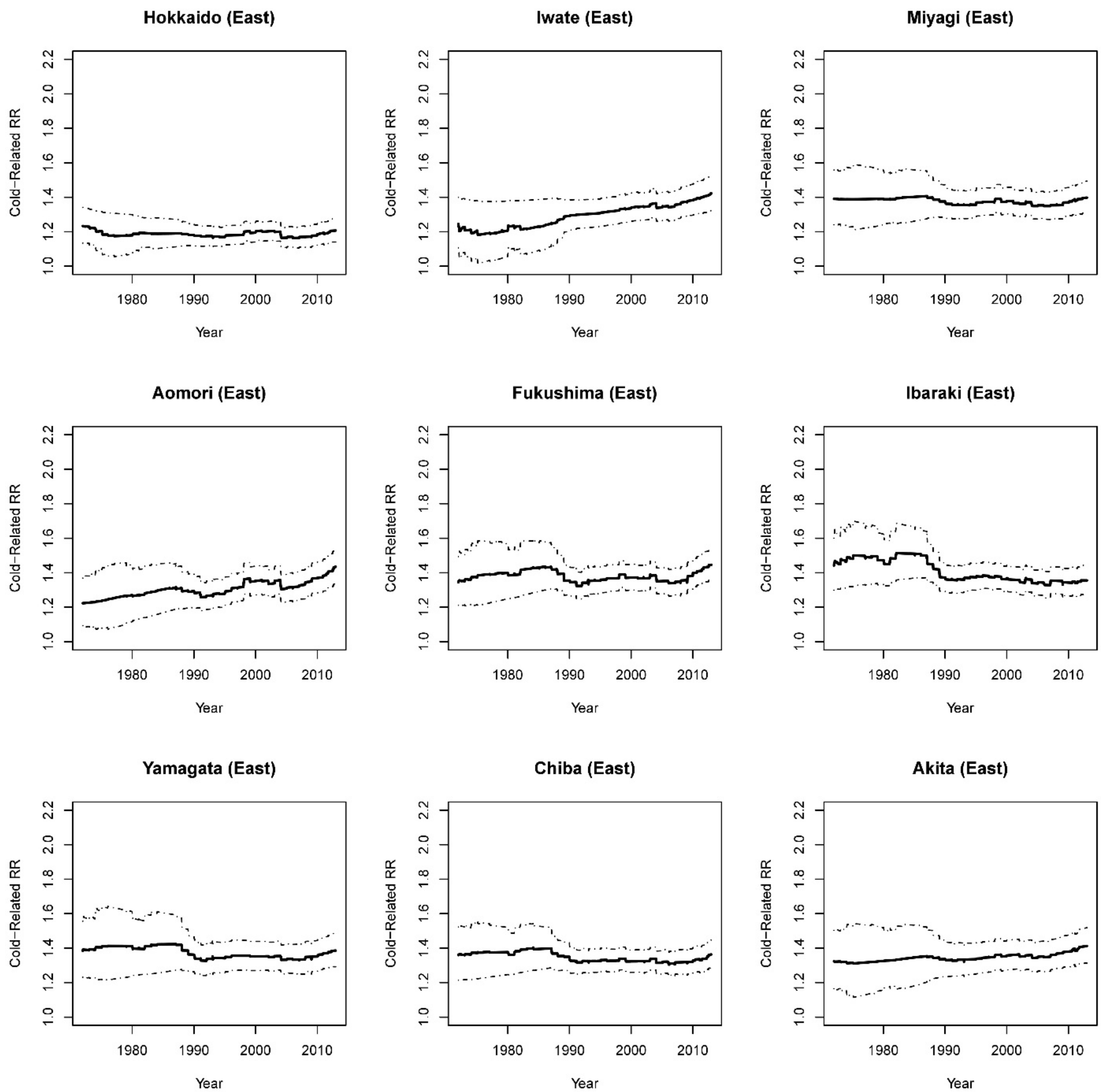
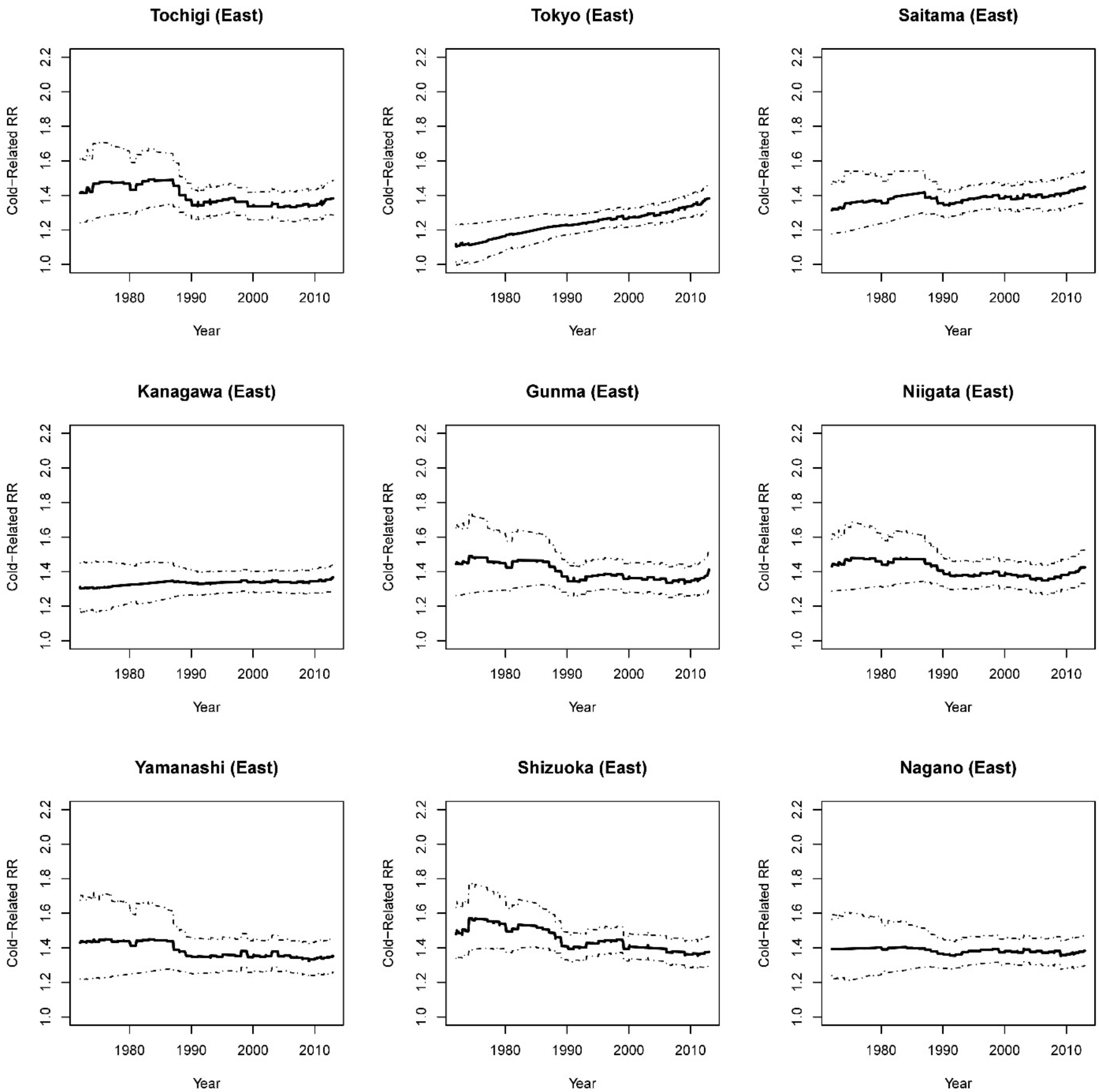

Nagasaki (West)
Heat−Related RR
0.8
1.0
1.2
1.4
1980
1990
2000
2010
Year
Okinawa (West)
Heat−Related RR
0.8
1.0
1.2
1.4
1980
1990
2000
2010
Year

Figure S7. Prefecture-specific time-varying cold-related mortality risk. The cold-related risk was defined as the relative risk comparing the time-varying minimum mortality temperature (MMT) and the time-varying 1st temperature percentile. Black solid and dashed lines indicate the point estimate of the heat risk and 95% point-wise confidence intervals, respectively.





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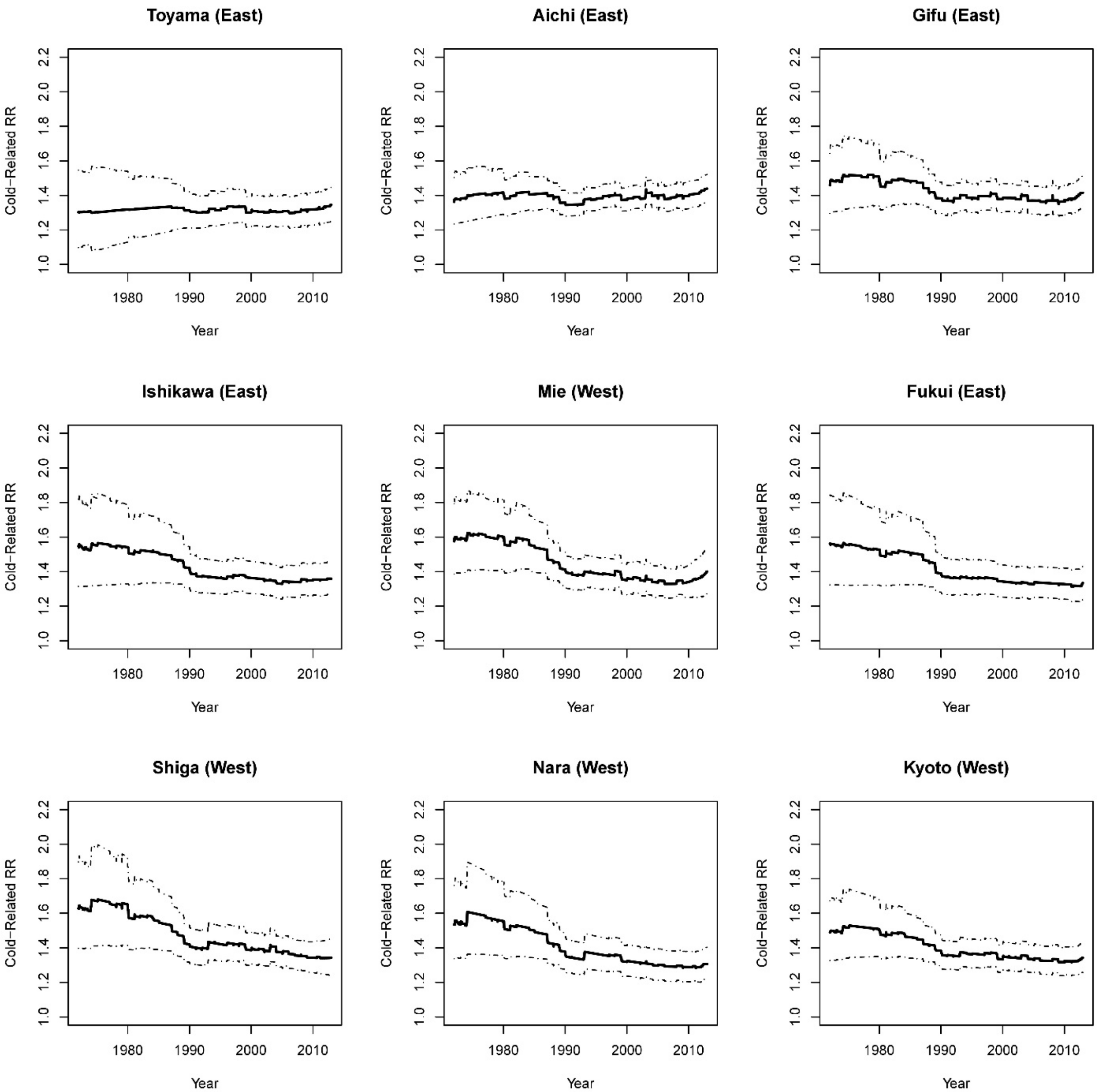
Tokyo (East)
Saitama (East)
Kanagawa (East)
Gunma (East)
Niigata (East)
Yamanashi (East)
Shizuoka (East)
Nagano (East)
Cold−Related RR
1.0
1.2
1.4
1.6
1.8
2.0
2.2
Year
1980
1990
2000
2010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Gifu (East)
Ishikawa (East)
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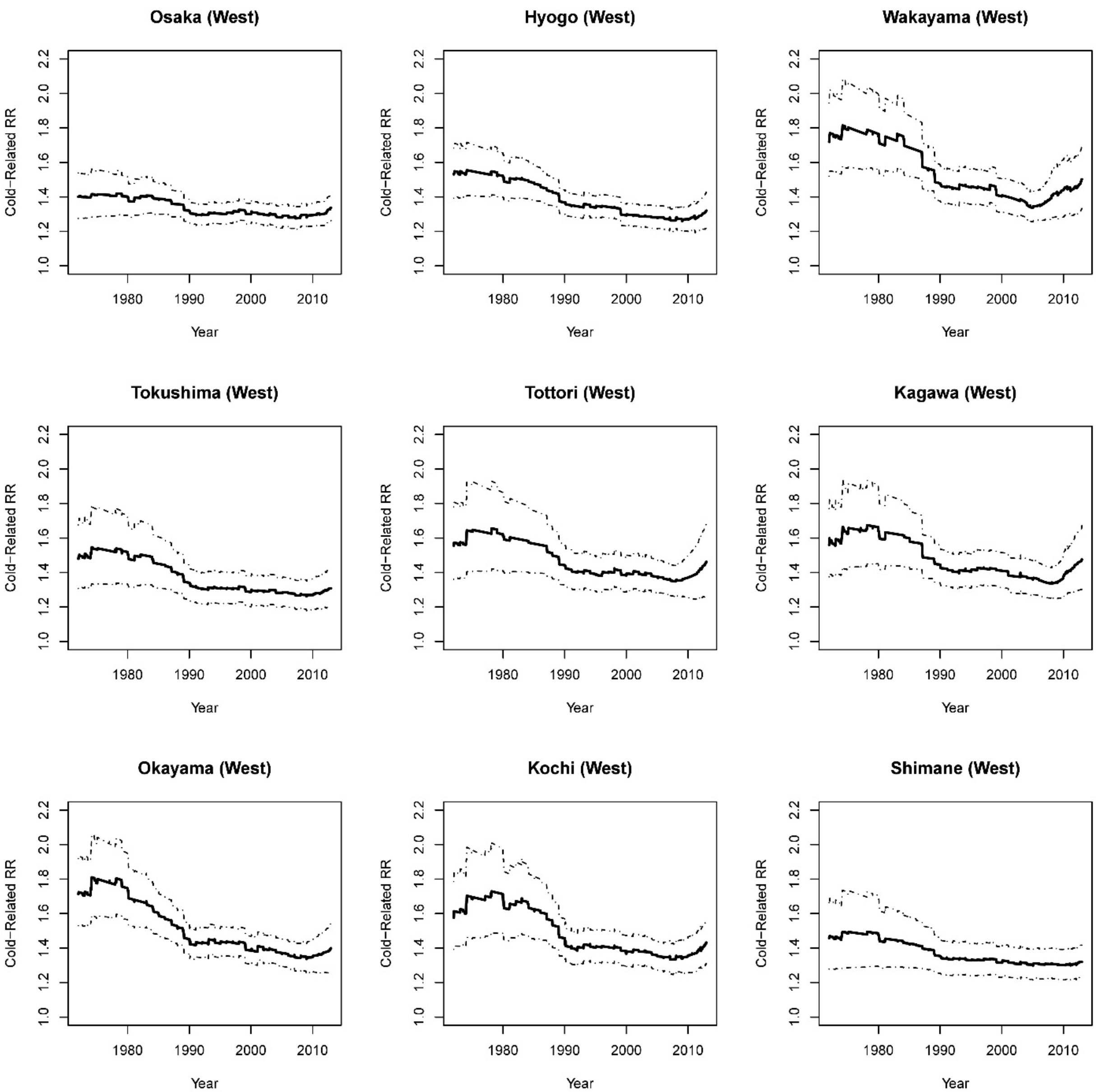
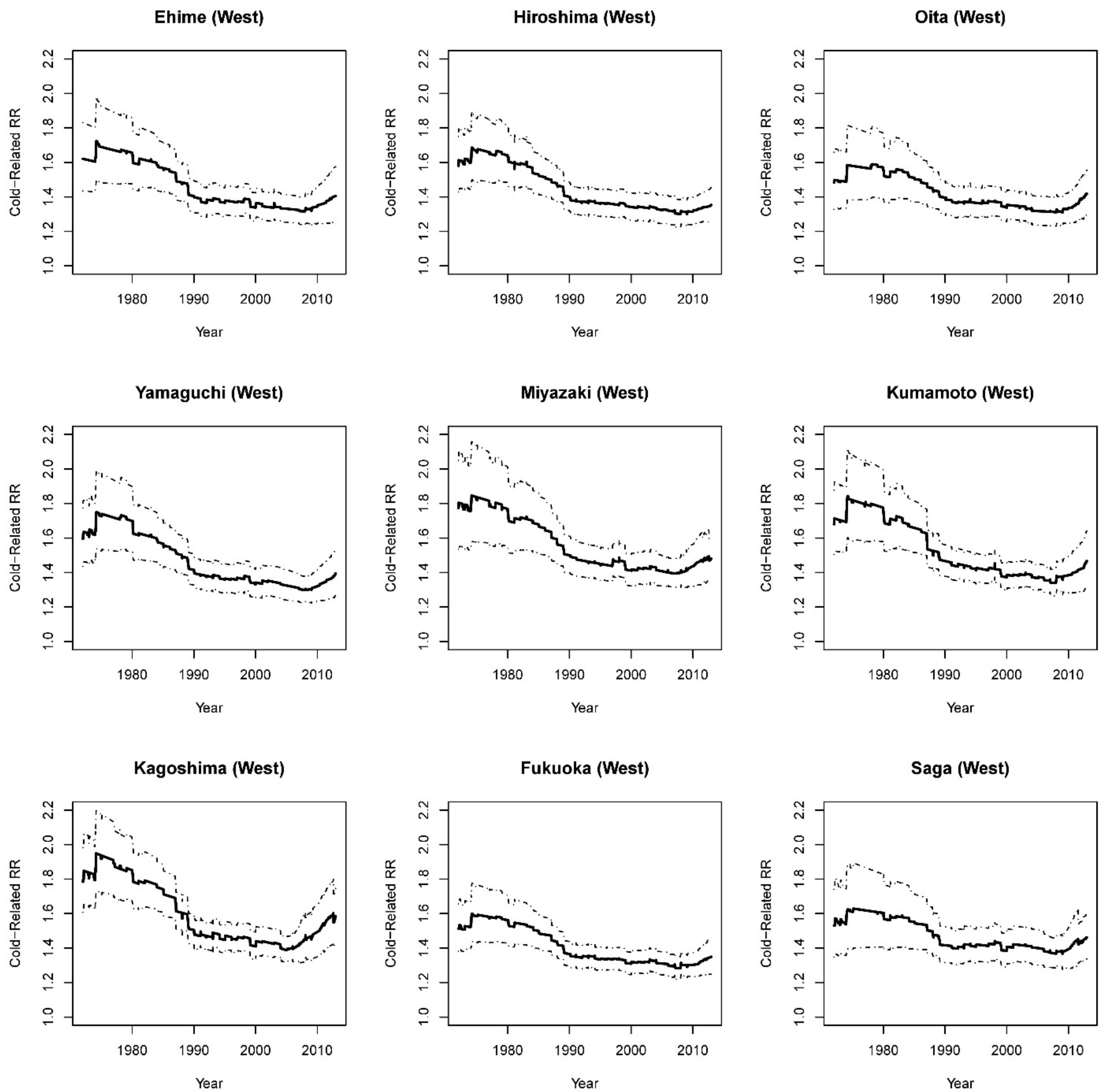
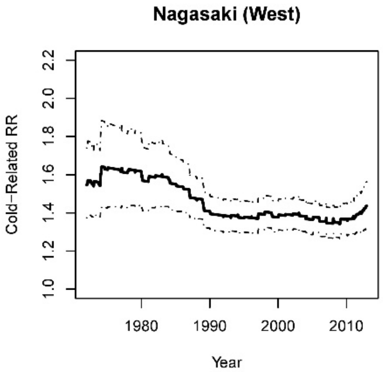
Shiga (West)
Nara (West)
Kyoto (West)
Cold−Related RR
Year
1.0
1.2
1.4
1.6
1.8
2.0
2.2
1980
1990
2000
2010



Osaka (West)
Hyogo (West)
Wakayama (West)
Tokushima (West)
Tottori (West)
Kagawa (West)
Okayama (West)
Kochi (West)
Shimane (West)
Cold−Related RR
Year
1.0
1.2
1.4
1.6
1.8
2.0
2.2
1980
1990
2000
2010



Ehime (West)
Hiroshima (West)
Oita (West)
Yamaguchi (West)
Miyazaki (West)
Kumamoto (West)
Kagoshima (West)
Fukuoka (West)
Saga (West)
Cold−Related RR
1.0
1.2
1.4
1.6
1.8
2.0
2.2
1980
1990
2000
2010
Year


Nagasaki (West)
Cold–Related RR
Year
1.0
1.2
1.4
1.6
1.8
2.0
2.2
1980
1990
2000
2010

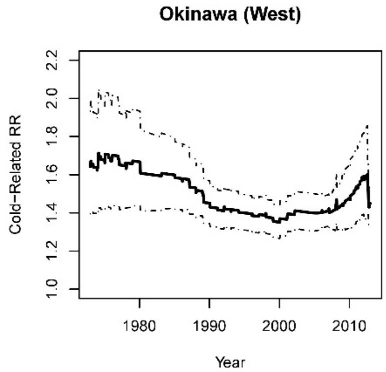
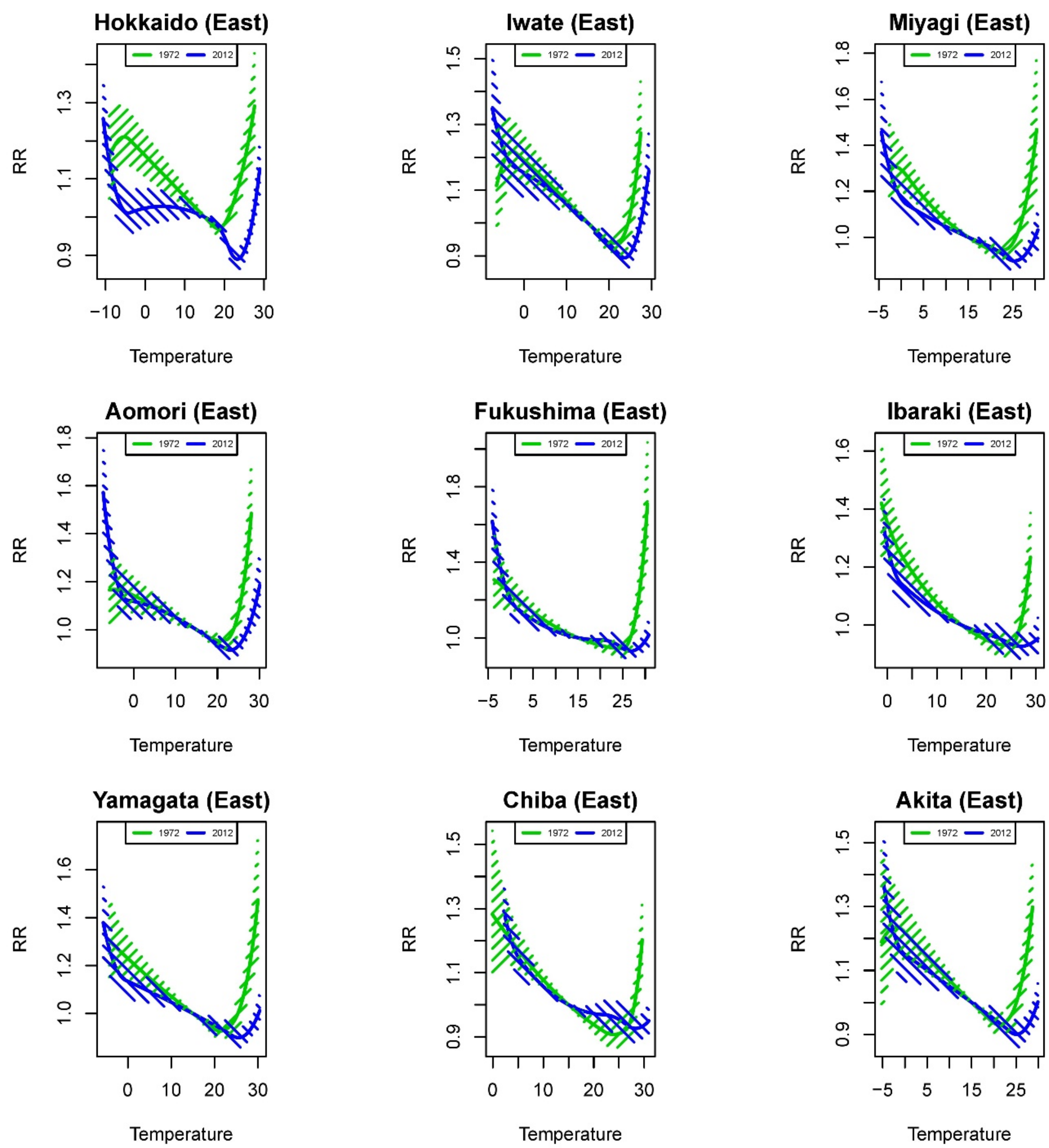
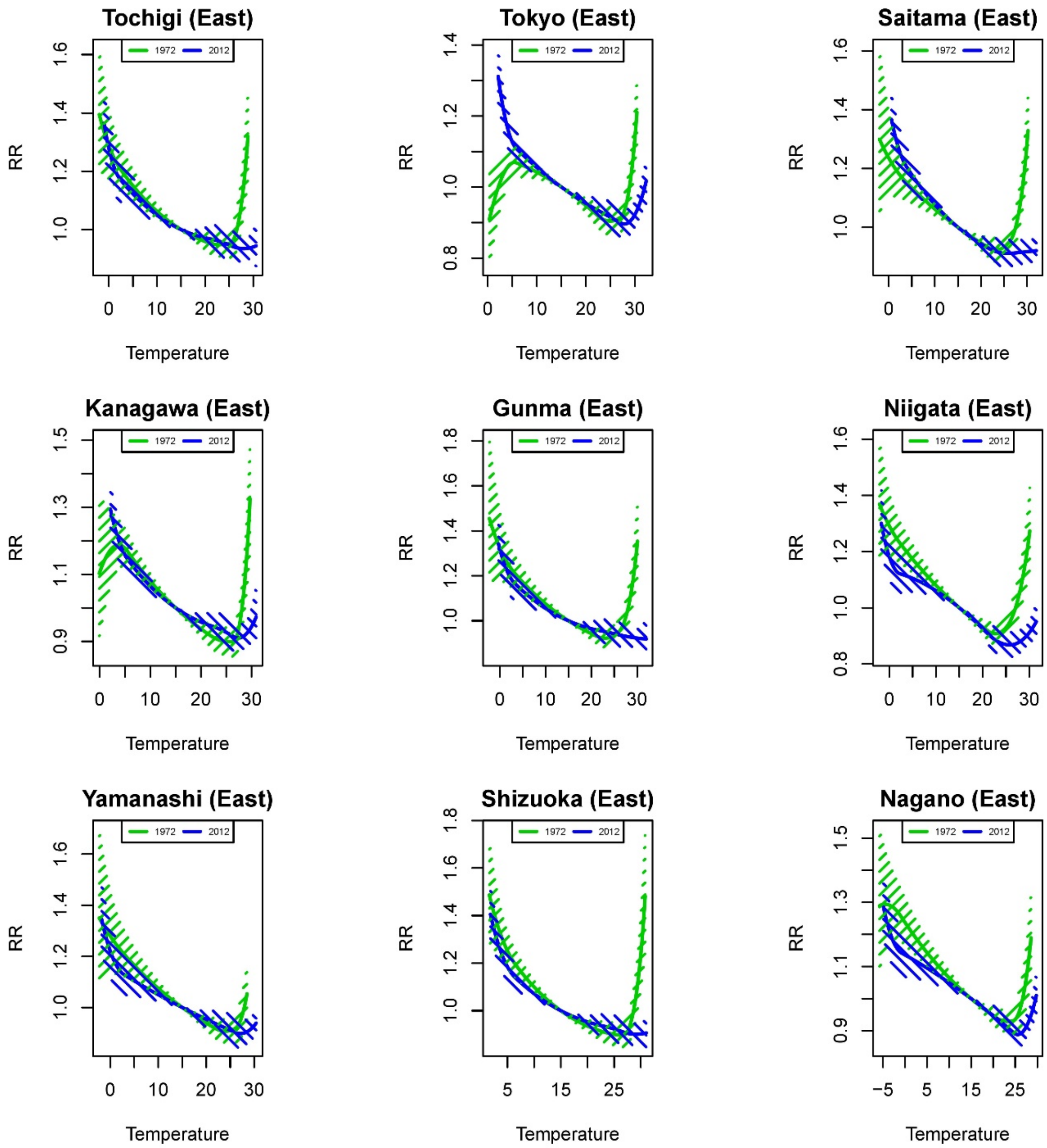
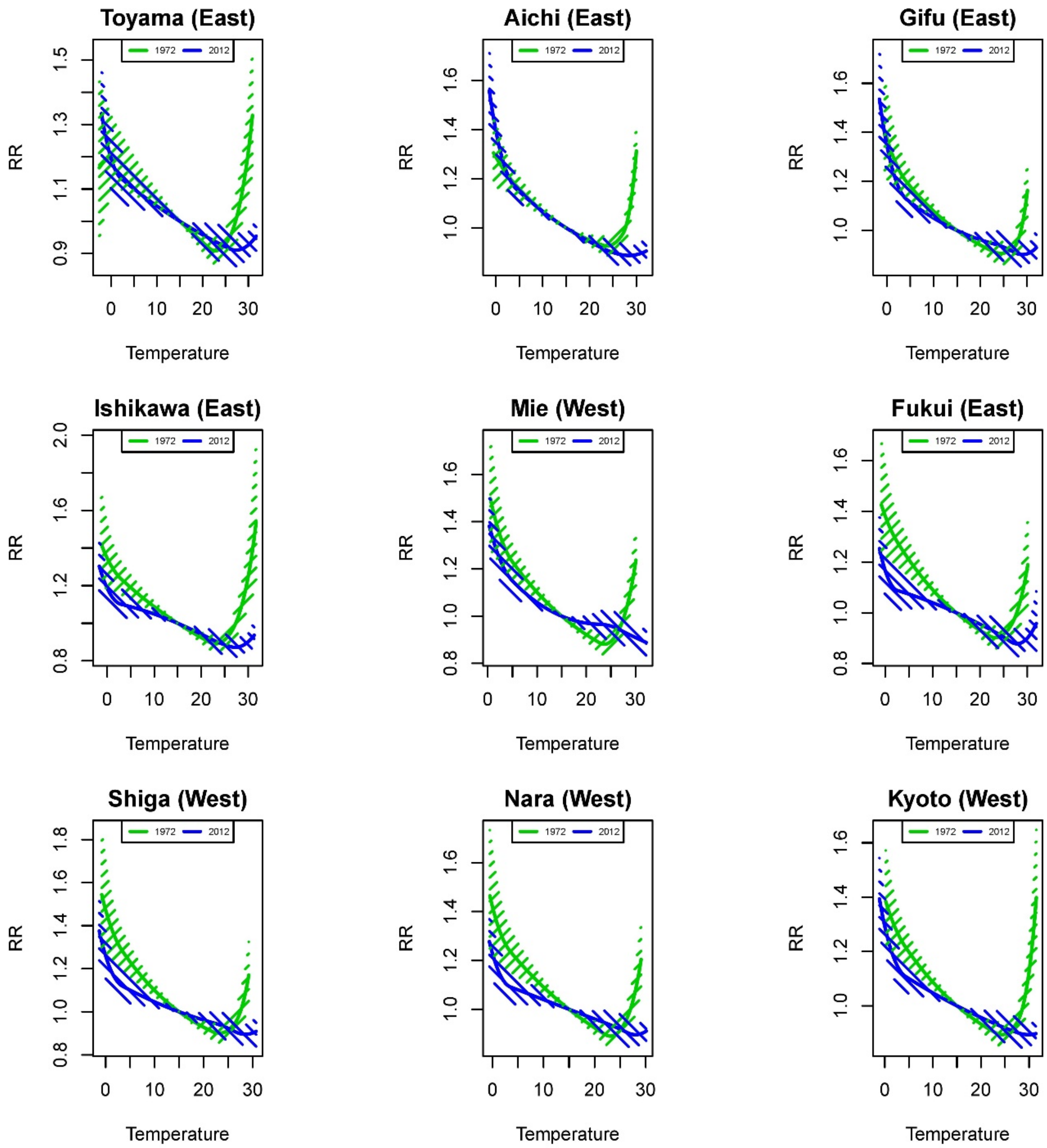

Okinawa (West)
Cold–Related RR
Year
1.0
1.2
1.4
1.6
1.8
2.0
2.2
1980
1990
2000
2010

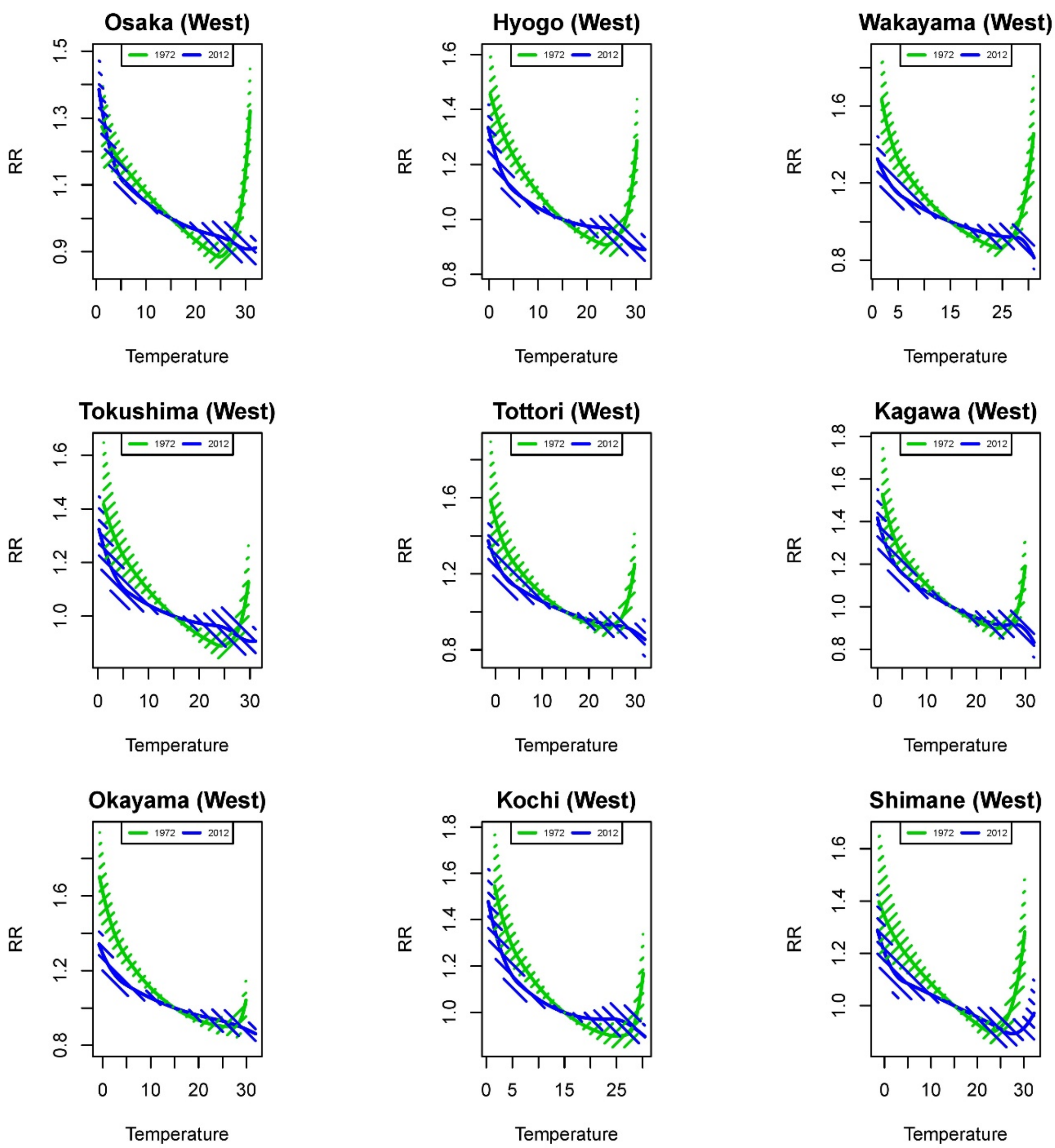
Figure S8. Prefecture-specific lag-cumulative relative risk (RR) curve at the first/last years (1972/2012) of the study period. Green and blue sold lines with shaded areas indicate the estimated RR curves with 95% confidence regions in 1972 and in 2012, respectively.



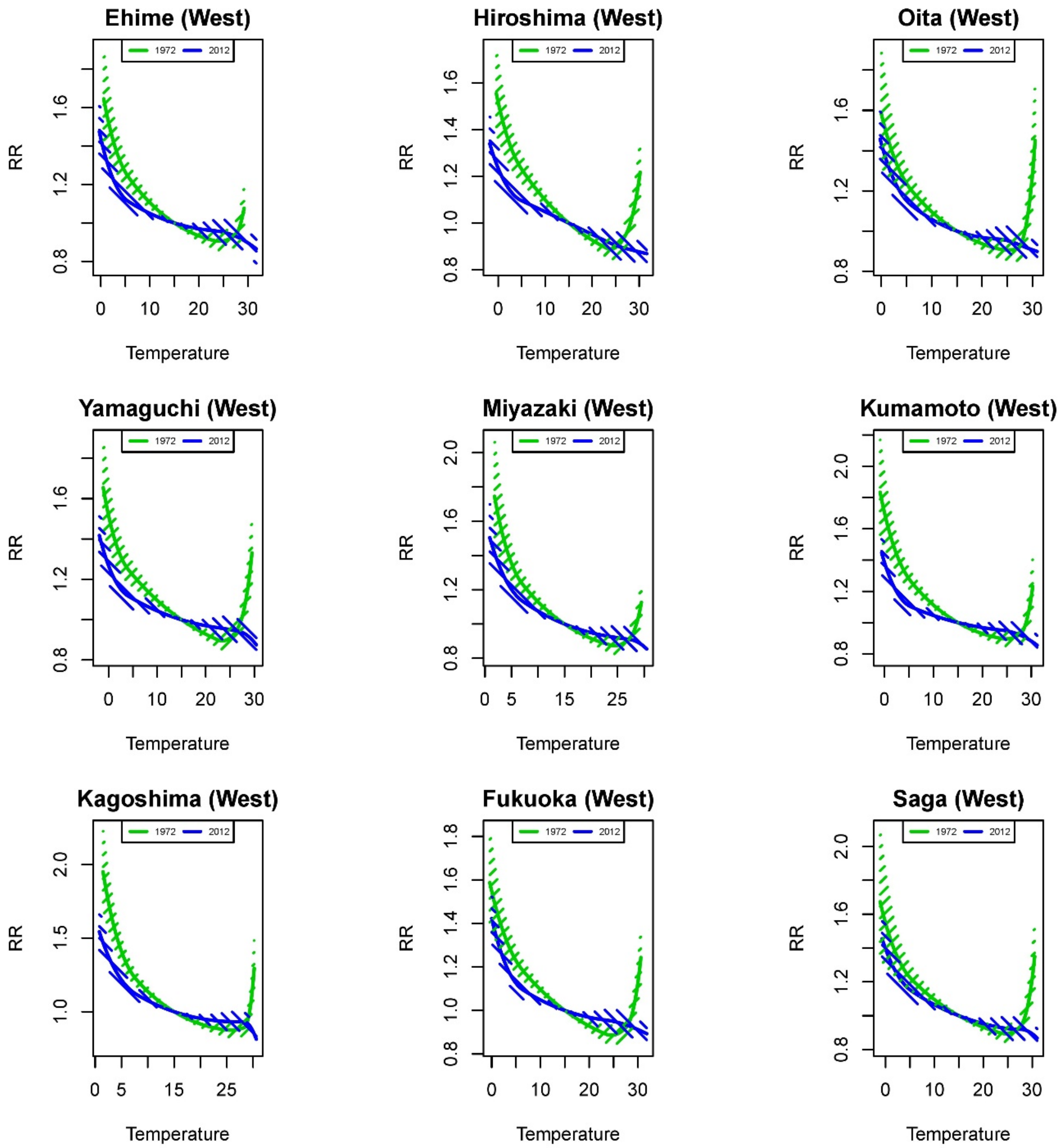

Tochigi (East)
Tokyo (East)
Saitama (East)
Kanagawa (East)
Gunma (East)
Niigata (East)
Yamanashi (East)
Shizuoka (East)
Nagano (East)
1972
2012
RR
Temperature



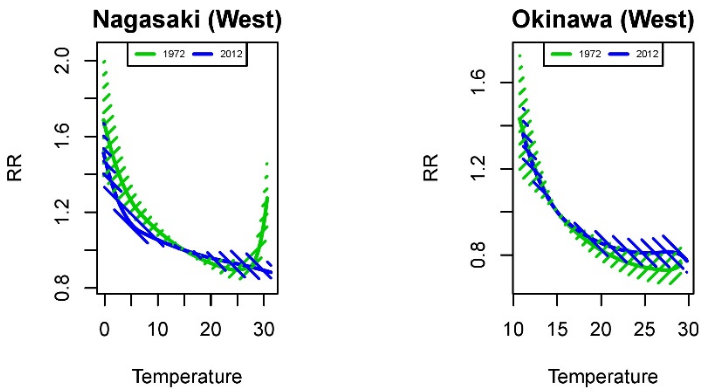
Toyama (East)
Aichi (East)
Gifu (East)
Ishikawa (East)
Mie (West)
Fukui (East)
Shiga (West)
Nara (West)
Kyoto (West)
1972
2012
RR
Temperature



Osaka (West)
Hyogo (West)
Wakayama (West)
Tokushima (West)
Tottori (West)
Kagawa (West)
Okayama (West)
Kochi (West)
Shimane (West)
1972
2012
RR
Temperature



Ehime (West)
Hiroshima (West)
Oita (West)
Yamaguchi (West)
Miyazaki (West)
Kumamoto (West)
Kagoshima (West)
Fukuoka (West)
Saga (West)
1972
2012
RR
Temperature



Nagasaki (West)
1972
2012
RR
2.0
1.6
1.2
0.8
0
10
20
30
Temperature
Okinawa (West)
1972
2012
RR
1.6
1.2
0.8
10
15
20
25
30
Temperature

Figure S9. Gender-specific time-varying minimum mortality temperature (MMT) together with the time-varying minimum mortality temperature percentile (MMTP) (top), time-varying heat-related mortality risk (middle), and time-varying cold-related mortality risk (bottom). Black solid and dashed lines indicate the point estimate of the MMT and 95% point-wise confidence intervals, respectively. Blue line in the top panels indicates the MMTP.

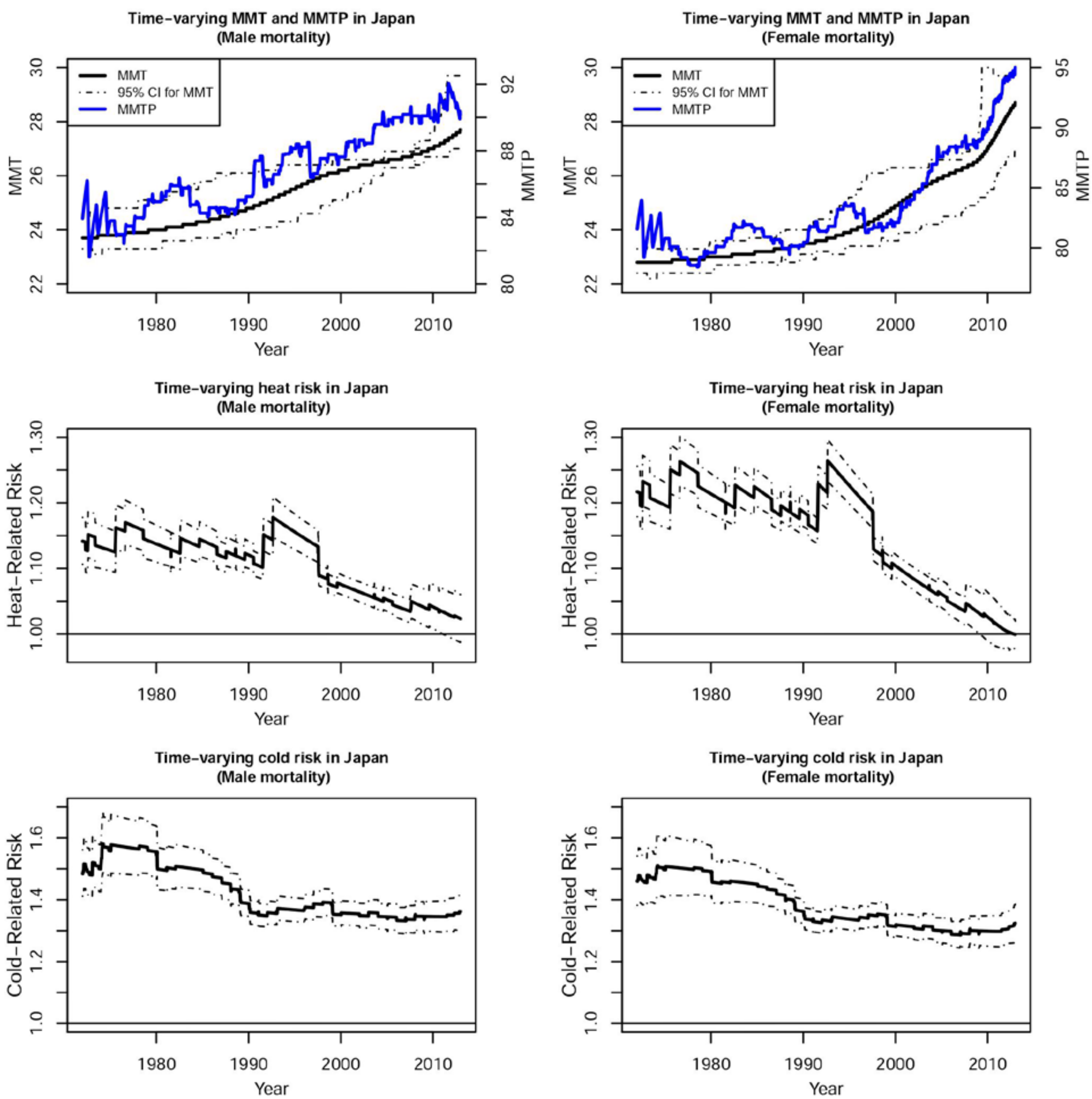


Figure S10. Cause-specific time-varying minimum mortality temperature (MMT) together with the time-varying minimum mortality temperature percentile (MMTP) (top), time-varying heat-related mortality risk (middle), and time-varying cold-related mortality risk (bottom). Black solid and dashed lines indicate the point estimate of the MMT and 95% point-wise confidence intervals, respectively. Blue line in the top panels indicates the MMTP.