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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Lay CR, Sarofim MC, Vodonos Zilberg A, et al. City-level vulnerability to temperature-related mortality in the USA and future projections: a geographically clustered meta-regression. *Lancet Planet Health* 2021; published online May 19. http://dx.doi.org/10.1016/S2542-5196(21)00058-9.

Supplemental Information

Adaptive Human Health Heat-Mortality Behavior in the United States

Lay et al.

Detailed methods for exposure response function (*ERF*) fitting

To quantify trends in adaptation over time, we fit ERFs separately in four time periods (1973-1982, 1983-1992, 1993-2002, and 2003-2013). The regressions defining the ERFs included terms for both the daily (lag 0) and the five-day moving average (MA15) of daily mean temperature. We used daily mean temperature rather than a relative scale of percentiles that encompassed all locations to aid in projections using modeled temperatures from GCM. We chose MA15 for concordance with a previous study (Nordio et al. 2015), and to reduce the complexity of the model and improve power. MA15 generally captures cold-related mortality (Braga et al. 2002, Nordio et al. 2015), while lag 0 generally captures heat effects (e.g., Vicedo-Cabrera et al. 2019). However, since heat waves over several days can also result in increased mortality, MA15 was included as a predictor across the range of temperatures. We performed this analysis in two stages (Nordio et al. 2015), to produce meta-smoothed spline coefficients for mortality due to lag 0 (β_{t0}) and MA15 (β_{t5}) temperatures for each cluster and time period.

In the first stage, we identified appropriate knot locations for each temperature term (lag 0 and MA15) within each cluster as follows. For each city (i) in each time period (p), we fit two over-dispersed Poisson (quasi-Poisson) generalized additive models (GAMs) to determine the exposure-response functions (ERFs) for temperature and mortality (Equations S-1 and S-2):

$$\log(\mu_t) = \beta_0 + \beta_w DOW_t + \beta_s ns(time_t, 6) + \beta_{t0}\, bs(T_{lag0}, 2) + \varepsilon_t \quad \text{(S-1)}$$

$$\log(\mu_t) = \beta_0 + \beta_w DOW_t + \beta_s ns(time_t, 6) + \beta_{t5}\, bs(T_{MA15}, 2) + \varepsilon_t \quad \text{(S-2)}$$

Where DOW_t is a factor representing day of the week; and $ns(time_t, 6)$ is a natural spline representing the day within the modeled time period, which has knots positioned at two-month intervals to represent seasonal variation as well as changes in overall mortality over the time period. β_0 is the intercept and the other βs represent the regression coefficients for each associated term. We fit all regressions using *dlnm* (Gasparrini 2011) in R (R Core Team 2019).

Both temperature terms (T_{lag0} and T_{MA15}) were modeled as basis splines (bs) with two degrees of freedom containing k total knots, k-2 interior knots, and two boundary knots. We centered the splines for both terms at 15·6°C (Anderson and Bell 2009). Boundary knots represented the mean of the range of temperatures observed in all cities within a cluster and period. We determined the number and location of interior knots for each cluster and time period by fitting models with knots at varying percentiles from 5 to 95, and compared the quasi-likelihood based on Akaike's Information Criterion (Q-AIC) for each model for all cities in the clusters (Peng et al. 2006). Interior knot locations are thus the same among cities within the same cluster and time period, but are different among clusters.

In the second stage, after identifying the appropriate knot locations for each spline term within each cluster and time period, we fit the final models for each city and time period. The final model contained both the T_{lag0} and T_{MA15} terms. We then combined city-specific estimates for heat-related mortality in each time period into cluster-level estimates through meta-smoothing with the *mvmeta* package (Gasparrini et al. 2012, Nordio et al. 2015, Equation S-3):

$$\log(\mu_t) = \beta_0 + \beta_w DOW_t + \beta_s ns(time_t, 6) + \beta_{t0}\, bs(T_{lag0}, 2) + \beta_{t5}\, bs(T_{MA15}, 2) + \varepsilon_t \quad \text{(S-3)}$$

This resulted in meta-smoothed spline coefficients for mortality due to lag 0 (β_{t0}) and MA15 (β_{t5}) temperatures for each cluster in each of the four time periods.

Table S-1. City composition of clusters*

Cluster	Cities						
	ALLENTOWN (PA)	CARLISLE (PA)	HARTFORD (CT)	NEW LONDON (CT)	PLYMOUTH (MA)	STAMFORD (CT)	··
	ANNANDALE (VA)	DOVER (DE)	JERSEY CITY (NJ)	NEW YORK (NY)	PROVIDENCE (RI)	TOMS RIVER (NJ)	··
	ATLANTIC CITY (NJ)	ELIZABETH (NJ)	LANCASTER (PA)	NEWARK (NJ)	READING (PA)	TRENTON (NJ)	··
1	BALTIMORE (MD)	ESSEX (MA)	MELVILLE (NY)	NEWBURGH (NY)	**RICHMOND (VA)**	UPPER MARLBORO (MD)	··
	BARNSTABLE (MA)	GETTYSBURG (PA)	MIDDLESEX (NJ)	PATERSON (NJ)	ROCKVILLE (MD)	WILMINGTON (DE)	··
	BOSTON (MA)	HARRISBURG (PA)	NEW HAVEN (CT)	PHILADELPHIA (PA)	SPRINGFIELD (MA)	YORK (PA)	··
	AKRON (OH)	BURLINGTON (VT)	DETROIT (MI)	GRAND RAPIDS (MI)	LOGAN (UT)	OMAHA (NE)	STATE COLLEGE (PA)
	ALBANY (NY)	CANTON (OH)	ELKHART (IN)	GREEN BAY (WI)	MADISON (WI)	OTTAWA (IL)	TOLEDO (OH)
	ANN ARBOR (MI)	CEDAR RAPIDS (IA)	ERIE (PA)	HOLLAND (MI)	MERCER (PA)	PORTAGE (IN)	WORCESTER (MA)
	BANGOR (ME)	CHICAGO (IL)	FARGO (ND)	IOWA CITY (IA)	MILWAUKEE (WI)	PORTLAND (ME)	YOUNGSTOWN (OH)
2	BATH (NY)	COLORADO SPRINGS (CO)	FLINT (MI)	KALAMAZOO (MI)	MINNEAPOLIS (MN)	ROCHESTER (NY)	··
	BEAVER DAM (WI)	DAVENPORT (IA)	FORT WAYNE (IN)	KENOSHA (WI)	MUSKEGON (MI)	SCRANTON (PA)	··
	BOULDER (CO)	DENVER (CO)	GARY (IN)	LA PORTE (IN)	NASHUA (NH)	SIOUX CITY (IA)	··
	BUFFALO (NY)	DES MOINES (IA)	GRAND HAVEN (MI)	LANSING (MI)	NILES (MI)	SOUTH BEND (IN)	··
	CHARLESTON (WV)	DAYTON (OH)	INDIANAPOLIS (IN)	MADISON (IL)	SPRINGFIELD (MO)	TERRE HAUTE (IN)	WICHITA (KS)
3	CINCINNATI (OH)	EAST ST. LOUIS (IL)	KANSAS CITY (KS)	MIDDLETOWN (OH)	ST. CHARLES (MO)	TOPEKA (KS)	··
	CLEVELAND (OH)	EVANSVILLE (IN)	LAFAYETTE (IN)	MUNCIE (IN)	**ST. LOUIS (MO)**	WASHINGTON (DC)	··
	COLUMBUS (OH)	GREENSBURG (PA)	LOUISVILLE (KY)	PITTSBURGH (PA)	STEUBENVILLE (OH)	WASHINGTON (PA)	··
	ATLANTA (GA)	CHARLOTTE (NC)	DURHAM (NC)	GREENVILLE (SC)	MACON (GA)	NASHVILLE (TN)	SPARTANBURG (SC)
	AUGUSTA (GA)	CHATTANOOGA (TN)	FAYETTEVILLE (NC)	HICKORY (NC)	MEMPHIS (TN)	**NORFOLK (VA)**	TULSA (OK)
4	BIRMINGHAM (AL)	COLUMBIA (SC)	FORT WORTH (TX)	KNOXVILLE (TN)	MONROE (LA)	OKLAHOMA CITY (OK)	WINSTON-SALEM (NC)
	CHARLESTON (SC)	DALLAS (TX)	GREENSBORO (NC)	LITTLE ROCK (AR)	MYRTLE BEACH (SC)	RALEIGH (NC)	··
	ANAHEIM (CA)	LOS ANGELES (CA)	RIVERSIDE (CA)	SAN FRANCISCO (CA)	STOCKTON (CA)	VENTURA (CA)	··
5	EUGENE (OR)	OAKLAND (CA)	SACRAMENTO (CA)	SAN JOSE (CA)	TACOMA (WA)	··	··
	EVERETT (WA)	PORTLAND (OR)	SAN DIEGO (CA)	SEATTLE (WA)	VANCOUVER (WA)	··	··
	AUSTIN (TX)	HOUSTON (TX)	LAKE CHARLES (LA)	NEW ORLEANS (LA)	PORT ARTHUR (TX)	··	··
6	BATON ROUGE (LA)	JACKSONVILLE (FL)	MOBILE (AL)	OCALA (FL)	SAN ANTONIO (TX)	··	··
	GAINESVILLE (FL)	LAFAYETTE (LA)	MONTGOMERY (AL)	PENSACOLA (FL)	TALLAHASSEE (FL)	··	··
	BROWNSVILLE (TX)	FORT LAUDERDALE (FL)	LAKELAND (FL)	MIAMI (FL)	SARASOTA (FL)	··	··
7	CORPUS CHRISTI (TX)	FORT MYERS (FL)	MCALLEN (TX)	ORLANDO (FL)	ST. PETERSBURG (FL)	··	··
	DAYTONA BEACH (FL)	FORT PIERCE (FL)	MELBOURNE (FL)	PALM BEACH (FL)	TAMPA (FL)	··	··
8	BAKERSFIELD (CA)	EL PASO (TX)	**LAS VEGAS (NV)**	PHOENIX (AZ)	VISALIA (CA)	··	··

Cluster	Cities						
	EL CENTRO (CA)	FRESNO (CA)	MODESTO (CA)	TUCSON (AZ)	..	..	..
9	ALBUQUERQUE (NM)	BOISE CITY (ID)	KLAMATH FALLS (OR)	MEDFORD (OR)	OGDEN (UT)	RENO (NV)	SPOKANE (WA)
	AZTEC (NM)	GRAND JUNCTION (CO)	LAYTON (UT)	NAMPA (ID)	PROVO (UT)	SALT LAKE CITY (UT)	..

* For 1982 to 1983, the following cities were dropped, as data suggested change in reporting that caused large increase in mortality counts unrelated to an actual change in mortality. Cluster 1: RICHMOND (VA), Cluster 3: ST. LOUIS (MO), Cluster 4: NORFOLK (VA), and Cluster 8: LAS VEGAS (NV).

Table S-2. Missing data percentage by cluster and year

Cluster	Cities	1973-1982	1983-1992	1993-2002	2003-2013
1	36	2·5%	0%	1.9%	26.3%
2	52	0%	0%	8.1%	30.7%
3	24	0%	0%	2.9%	24.8%
4	27	0%	0%	0%	35.4%
5	17	0%	0%	0%	44.3%
6	15	0%	0%	0%	49.1%
7	15	0%	0%	0%	58.2%
8	9	11.1%	0%	0%	44.7%
9	13	5.5%	0%	24.6%	45.8%

Table S-3. Cochran's Q, I2, AIC, and BIC from the meta-regression. Decade was treated as a factor with 1993-2003 as the reference period. Models included summer mean temperature (Summer), winter mean temperature (Winter), air conditioning (AC), total population of the largest county in a city in the decade (Population), population aged 65 and over in that count (Age65Up).

			Cochran's Q					
Cluster	**lag**	**Model Call**	**Q**	**df**	**p**	**I^2**	**AIC**	**BIC**
1	lag0	Intercept	1197	705	0.000	41.100	-1630	-1538
1	lag0	Intercept + Decade	963	690	0.000	28.368	-1682	-1522
1	lag0	Intercept + Summer + Decade + Population + Age65Up	851	675	0.000	20.699	-1728	-1500
1	lag0	Intercept + Decade + Population + Age65Up	949	680	0.000	28.380	-1670	-1464
1	lag0	Intercept + Decade + AC + Summer + AC:Summer	795	675	0.001	15.074	-1771	-1542
1	lag0	Intercept + Decade + AC + Summer	850	680	0.000	19.976	-1738	-1532
1	MA15	Intercept	1108	846	0.000	23.654	-2097	-1968
1	MA15	Intercept + Decade	1009	828	0.000	17.904	-2115	-1901
1	MA15	Intercept + Decade + Winter + Population + Age65Up	904	810	0.012	10.397	-2138	-1839
1	MA15	Intercept + Decade + Population + Age65Up	950	816	0.001	14.093	-2113	-1842
2	lag0	Intercept	1223	828	0.000	32.3	-1417	-1351
2	lag0	Intercept + Decade	1054	816	0.000	22.6	-1474	-1352
2	lag0	Intercept + Decade + AC + Summer	947	808	0.001	14.6	-1526	-1366
2	lag0	Intercept + Decade + AC + Summer + AC:Summer	909	804	0.006	11.6	-1550	-1371
2	lag0	Intercept + Summer + Decade + Age65Up	953	808	0.000	15.2	-1526	-1366
2	lag0	Intercept + Decade + Age65Up	1040	812	0.000	21.9	-1473	-1332
2	MA15	Intercept	1108	846	0.000	23.7	-2097	-1969
2	MA15	Intercept + Decade	1009	828	0.000	17.9	-2115	-1901
2	MA15	Intercept + Decade + Summer + Winter + Age65Up	913	810	0.007	11.3	-2130	-1831
2	MA15	Intercept + Decade + Age65Up	969	822	0.000	15.1	-2111	-1869
2	MA15	Intercept + Decade + Winter + Age65Up + Winter:Age65Up	912	810	0.007	11.2	-2130	-1831
3	lag0	Intercept	565	372	0.000	34.2	-799	-744
3	lag0	Intercept + Decade	475	360	0.000	24.2	-816	-713
3	lag0	Intercept + Summer + Decade + Age65Up	411	352	0.017	14.3	-823	-690
3	lag0	Intercept + Decade + Age65Up	417	356	0.014	14.7	-826	-709
3	lag0	Intercept + Decade + AC + Summer + AC:Summer	415	348	0.008	16.1	-815	-666
3	lag0	Intercept + Decade + AC + Summer	423	352	0.006	16.7	-818	-684

Cluster	lag	Model Call	Cochran's Q			I^2	AIC	BIC
			Q	df	p			
3	MA15	Intercept	392	372	0.231	5.0	-847	-792
3	MA15	Intercept + Decade	358	360	0.526	0.0	-851	-749
3	MA15	Intercept + Decade + Summer + Winter + Age65Up	345	348	0.537	0.0	-838	-689
3	MA15	Intercept + Decade + Age65Up	352	356	0.554	0.0	-848	-730
3	MA15	Intercept + Decade + Winter + Age65Up + Winter:Age65Up	342	348	0.578	0.0	-841	-692
4	lag0	Intercept	577	420	0.000	27.2	-836	-779
4	lag0	Intercept + Decade	501	408	0.001	18.5	-865	-759
4	lag0	Intercept + Decade + AC + Summer	477	400	0.005	16.2	-862	-725
4	lag0	Intercept + Decade + AC + Summer + AC:Summer	474	396	0.004	16.4	-857	-703
4	lag0	Intercept + AC + Summer + Decade + Population + Age65Up	469	392	0.004	16.5	-852	-682
4	lag0	Intercept + Decade + AC + Population + Age65Up	477	396	0.003	17.0	-856	-702
4	lag0	Intercept + Decade + Population + Age65Up	488	400	0.002	18.1	-859	-721
4	MA15	Intercept	513	420	0.001	18.1	-843	-787
4	MA15	Intercept + Decade	474	408	0.014	13.9	-855	-750
4	MA15	Intercept + Decade + Summer + Winter + AC + Age65Up	446	392	0.032	12.0	-848	-678
4	MA15	Intercept + Decade + AC + Age65Up	460	400	0.020	13.1	-851	-713
4	MA15	Intercept + Decade + Winter + Age65Up + Winter:Age65Up	454	396	0.023	12.8	-848	-694
6	lag0	Intercept	332	295	0.066	11.3	-554	-480
6	lag0	Intercept + Decade	301	280	0.186	7.0	-548	-418
6	lag0	Intercept + Decade + AC + Summer	292	270	0.176	7.4	-536	-370
6	lag0	Intercept + Decade + AC + Summer + AC:Summer	285	265	0.186	7.1	-533	-348
6	lag0	Intercept + Decade + Summer + Winter + AC	278	265	0.274	4.8	-540	-354
6	lag0	Intercept + Decade + AC + Population + Age65Up	288	265	0.158	8.0	-528	-343
6	lag0	Intercept + Decade + Population + Age65Up	295	270	0.139	8.6	-533	-366
6	MA15	Intercept	284	236	0.018	16.8	-433	-384
6	MA15	Intercept + Decade	257	224	0.067	12.7	-425	-334
6	MA15	Intercept + Decade + Summer + Winter + AC + Age65Up	228	208	0.166	8.7	-417	-271

Cluster	lag	Model Call	Cochran's Q			I²	AIC	BIC
			Q	df	p			
6	MA15	Intercept + Decade + Summer + Winter + AC	235	212	0.134	9.8	-420	-288
6	MA15	Intercept + Decade + AC	245	220	0.122	10.1	-428	-324
6	MA15	Intercept + Decade + Winter + Age65Up + Winter:Age65Up	235	212	0.137	9.6	-418	-286
7	lag0	Intercept	275	236	0.040	14.3	-566	-517
7	lag0	Intercept + Decade	243	224	0.185	7.8	-569	-478
7	lag0	Intercept + AC + Summer + Decade + Population + Age65Up	218	208	0.304	4.6	-560	-414
7	lag0	Intercept + Decade + AC + Summer + AC:Summer	220	212	0.344	3.5	-566	-434
7	lag0	Intercept + Summer + Decade + AC	224	216	0.341	3.6	-570	-452
7	lag0	Intercept + Decade + AC	237	220	0.201	7.3	-566	-461
7	lag0	Intercept + Decade + Population + Age65Up	235	216	0.173	8.3	-560	-442
7	MA15	Intercept	299	236	0.003	21.0	-538	-490
7	MA15	Intercept + Decade	266	224	0.027	15.9	-536	-445
7	MA15	Intercept + Decade + Summer + Winter + AC + Population + Age65Up	236	204	0.060	13.6	-521	-361
7	MA15	Intercept + Decade + Summer + Winter	242	216	0.108	10.8	-540	-422
7	MA15	Intercept + Decade + AC	265	220	0.020	17.1	-528	-424
7	MA15	Intercept + Decade + AC + Age65Up + AC:Age65Up	250	212	0.036	15.4	-525	-393
9	lag0	Intercept	199	204	0.593	0.0	-213	-167
9	lag0	Intercept + Decade	182	192	0.688	0.0	-203	-116
9	lag0	Intercept + AC + Summer + Decade + Population + Age65Up	218	208	0.304	4.6	-560	-414
9	lag0	Intercept + Decade + AC + Summer + AC:Summer	285	265	0.186	7.1	-533	-348
9	lag0	Intercept + Decade + AC + Summer + Winter + Population + Age65Up	146	172	0.924	0.0	-196	-43
9	lag0	Intercept + Decade + Summer + Winter	157	184	0.922	0.0	-210	-96
9	lag0	Intercept + Decade + AC	178	188	0.683	0.0	-198	-98
9	lag0	Intercept + Decade + Population + Age65Up	168	184	0.802	0.0	-199	-85
9	MA15	Intercept	172	204	0.951	0.0	-213	-166
9	MA15	Intercept + Decade	161	192	0.951	0.0	-199	-112
9	MA15	Intercept + Decade + Summer + Winter + Population + Age65Up	148	176	0.942	0.0	-180	-40
9	MA15	Intercept + Decade + Summer + Winter	151	184	0.963	0.0	-193	-79
9	MA15	Intercept + Decade + AC	158	188	0.943	0.0	-193	-93
9	MA15	Intercept + Decade + Winter + Age65Up + Winter:Age65Up	153	180	0.929	0.0	-183	-56

Table S-4. Central year of 11-year time periods anticipated to have average U.S. temperature increases of 1-6°C over temperature in the baseline period (1986-2005), and the range of years over which change is projected to occur. Not all climate models project a 4°C, 5°C, and 6°C change before the end of the century. Arrival times would be different for alternative RCPs.

GCM (RCP 8.5)	1°C	2°C	3°C	4°C	5°C	6°C
CanESM2	2011	2033	2048	2062	2076	2091
CCSM4	2011	2037	2059	2077	2091	··
GISS E2 R	2025	2052	2082	··	··	··
HadGEM2 ES	2013	2029	2044	2055	2064	2077
MIROC5	2017	2033	2050	2067	2081	··
GFDL CM3	2013	2032	2049	2061	2071	2087
Year Range (not centralized)	2006-2030	2027-2057	2039-2087	2050-2084	2059-2096	2072-2096

Figure S-1. Risk attributable to temperature centered at average daily temperature for each city from the 2003-2013 hindcast. The red dots represent mortality attributable to lag 0 temperature, the blue dots represent mortality attributable to MA15 temperature, and the violet dots represent the sum of the two.

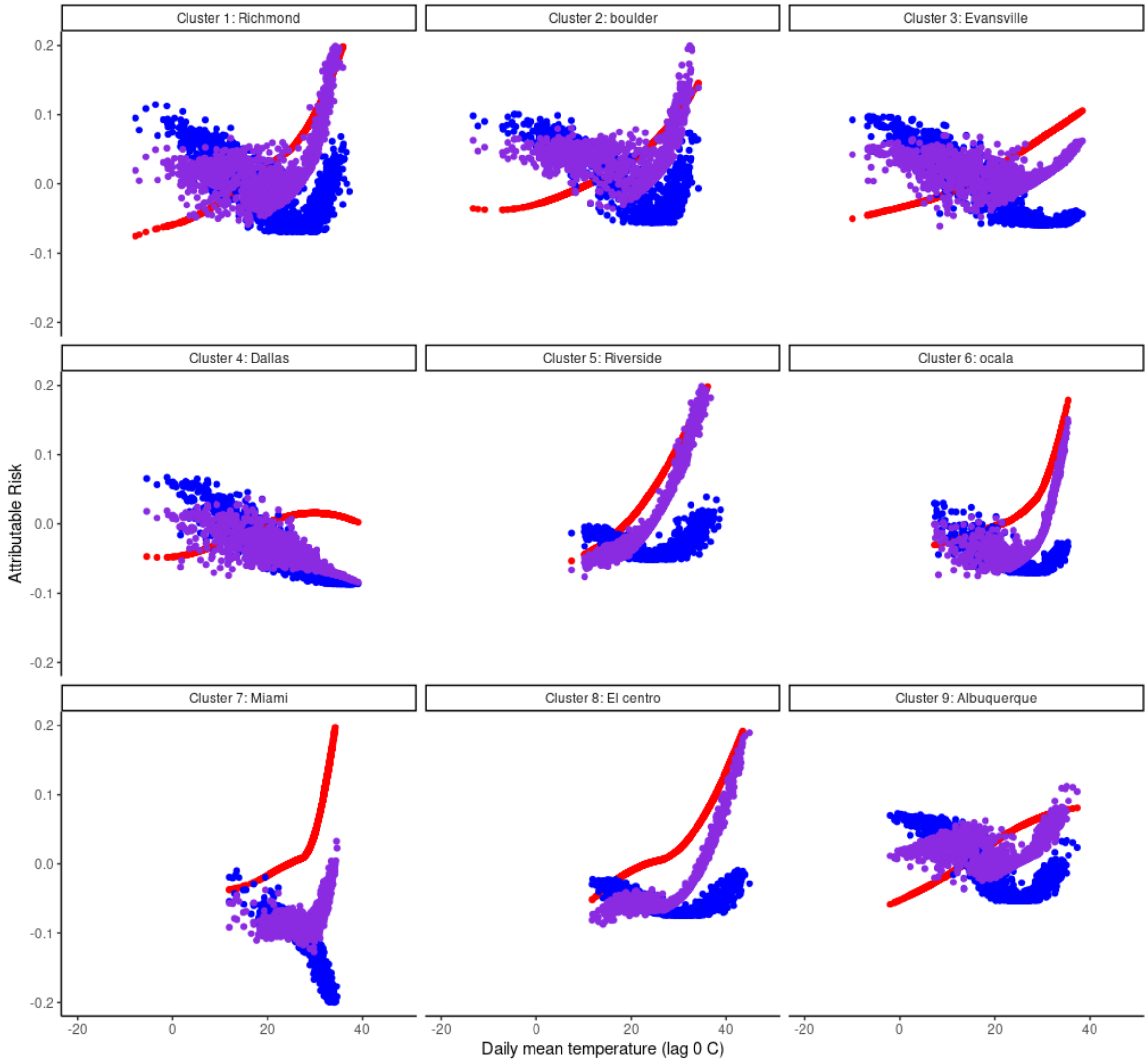


Figure S-2. Comparison of risk attributable to temperature for Cluster 1 at 1Δ°C and 6Δ°C. Warmer daily temperatures associated with warmer five-day moving average temperatures are associated with the highest risks for most clusters, but in Cluster 4, these produce the lowest risks.

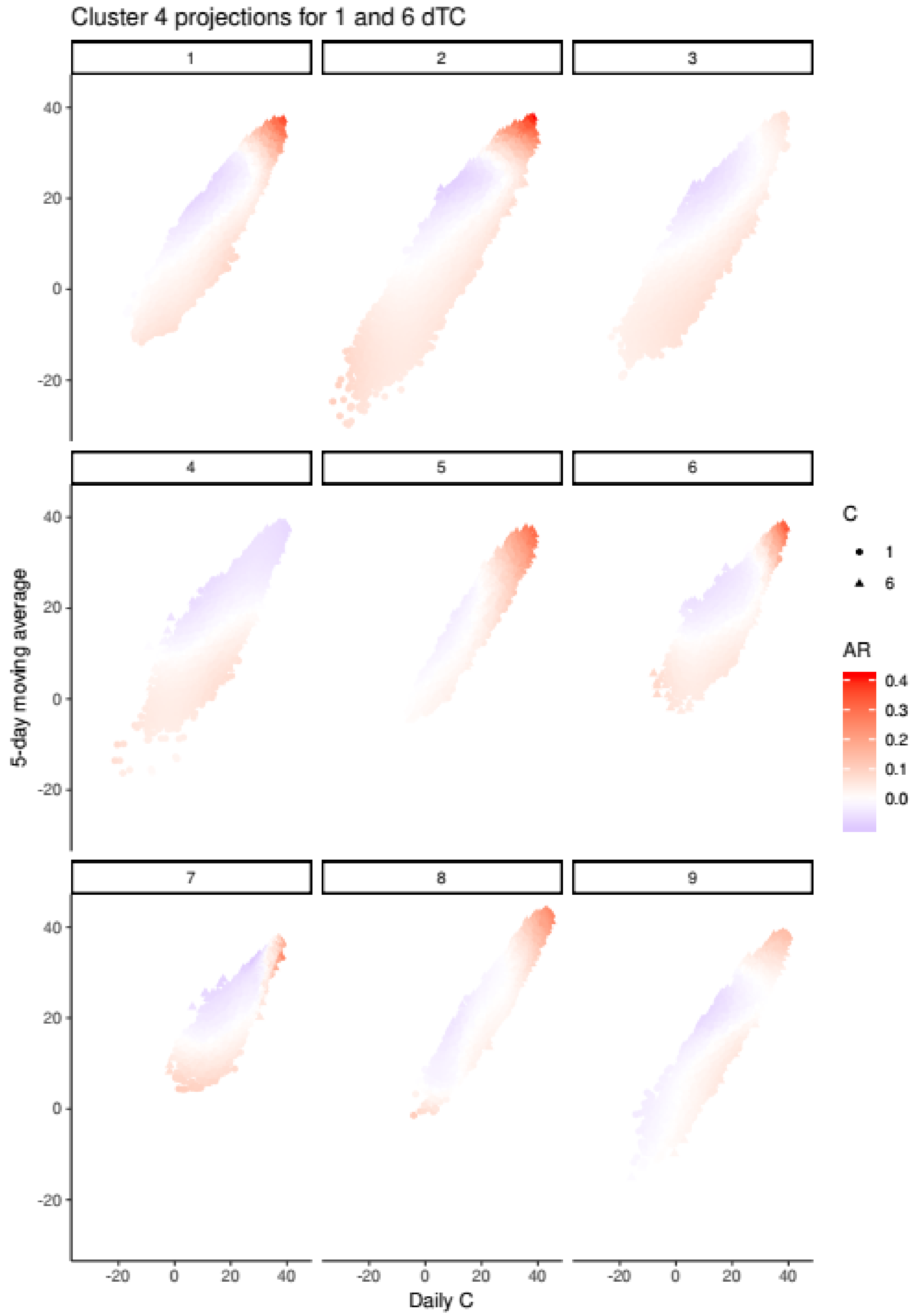
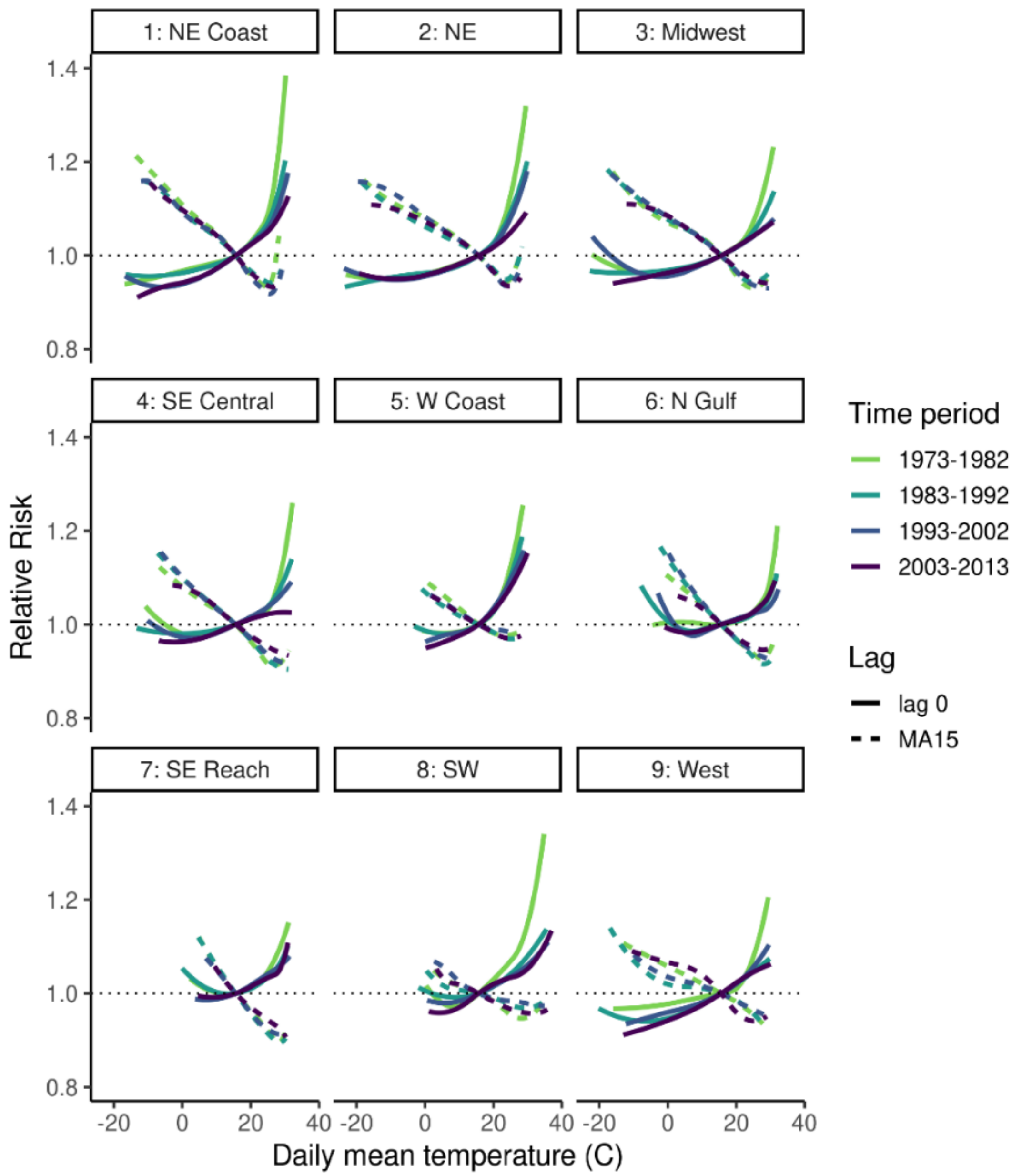


Figure S-3. ERF of relative risk for each cluster and temperature lag term, with curves centered at 15·6°C. The response to temperature changed over time for both lag 0 and MA15 ERFs.



Figures S-4. Change in attributable death relative to hindcast at 4Δ°C per 100,000 of 2010 population shown in relationship to temperature categories. "Coldest" temperatures are below the lowest bound for each cluster, "cold" temperatures are between the lowest bound and the lowest interior knot, "mid" temperatures are between the lowest and highest interior knots, "hot" temperatures are between the highest interior knot and the highest bound, and the "hottest" temperatures are above the highest bound. AN was calculated from the fitted splines from each historical time period. The effect of heat on increasing mortality is greatly reduced in 2003-2013 compared to earlier time periods.

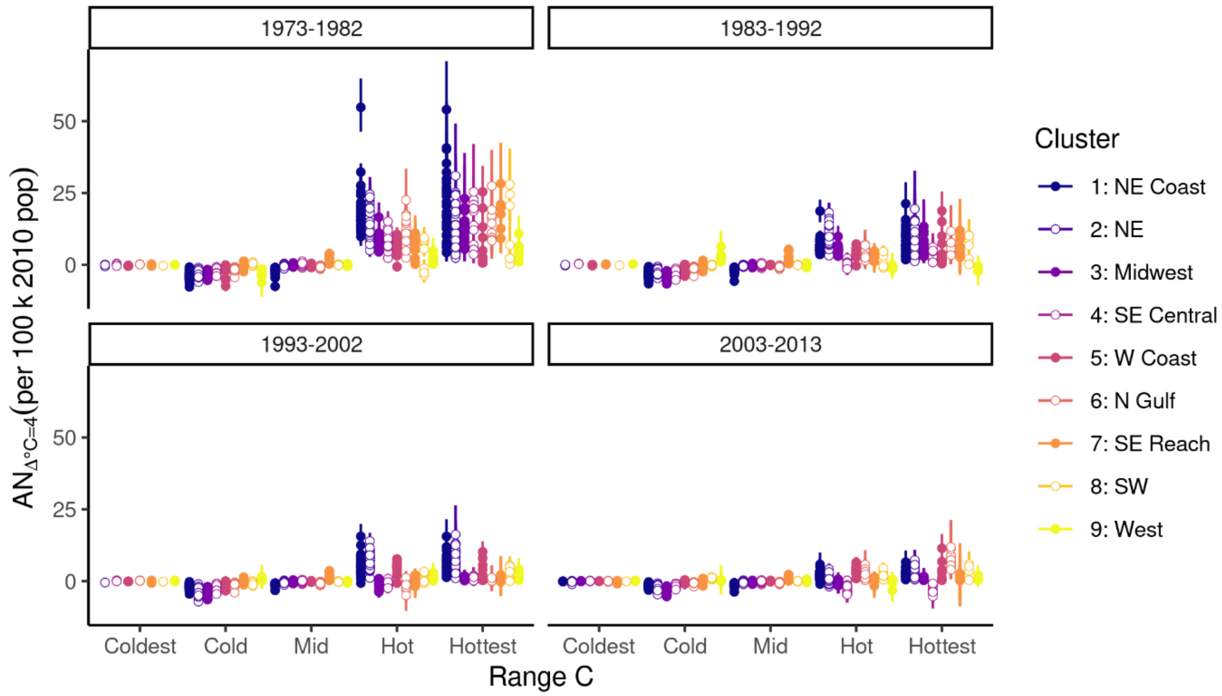


Figure S-5. Total change in attributable death relative to hindcast per 100,000 of 2010 population over a year by the historical period of fitted model at 3°ΔC (left) and 6°ΔC (right). Points represent the central estimate for each of the 208 cities, and whiskers represent the 66% confidence interval around those estimates.

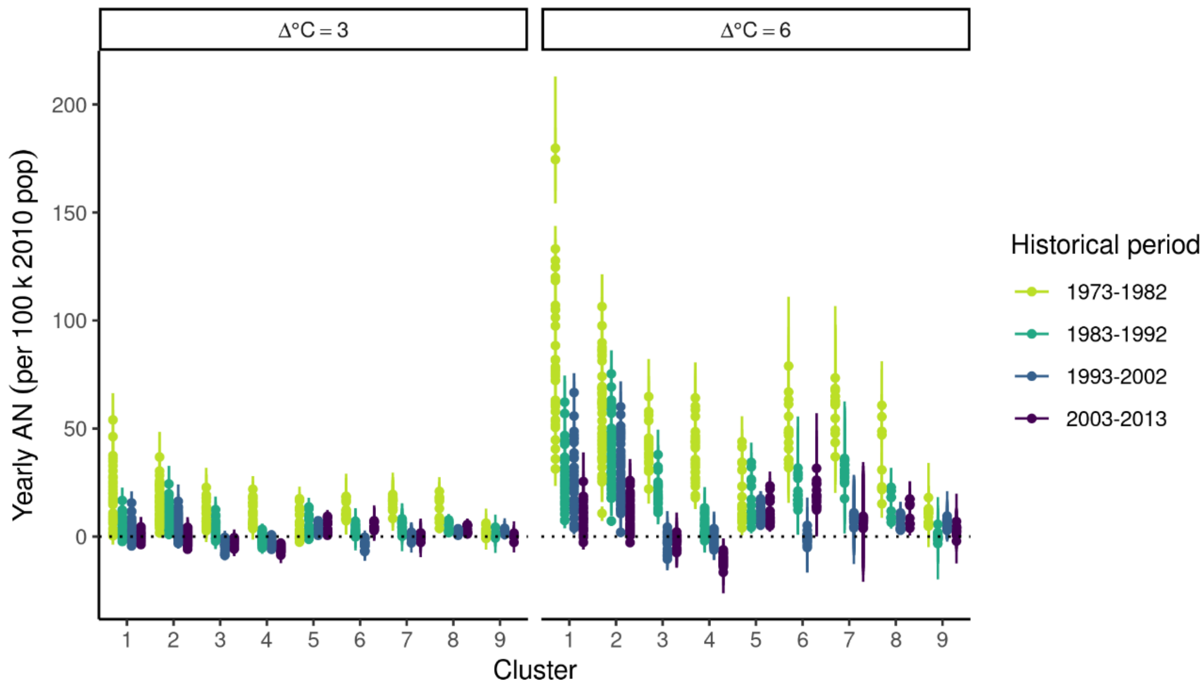


Figure S-6. Change in attributable mortality due to temperature, relative to 2010 population (per 100,000), shown by time period of historical data and cluster. Clusters 9 and 5 show relatively little evidence of adaptation compared to the other clusters.

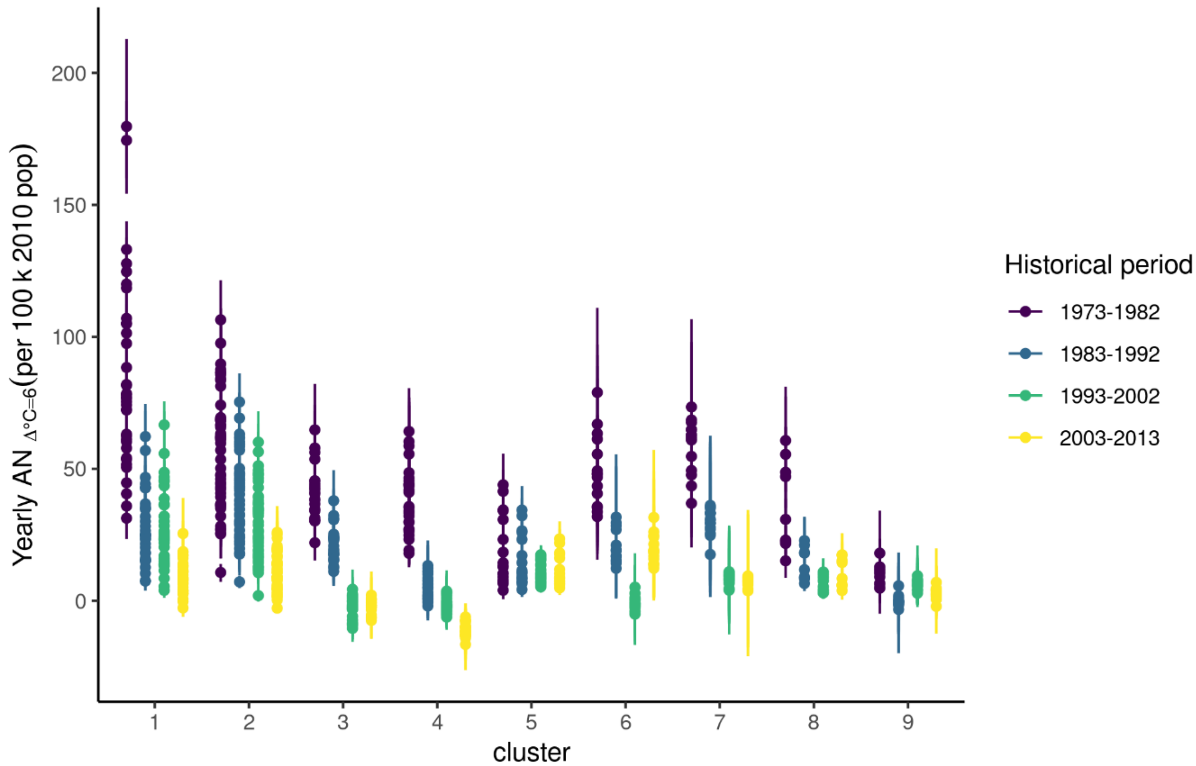


Figure S-7. Winter differences in attributable risk at 3°C change. Winter risk differs little from the hindcast overall, and, as expected, any differences do not appear related to air conditioning in the historical period in which the ERF was fit.

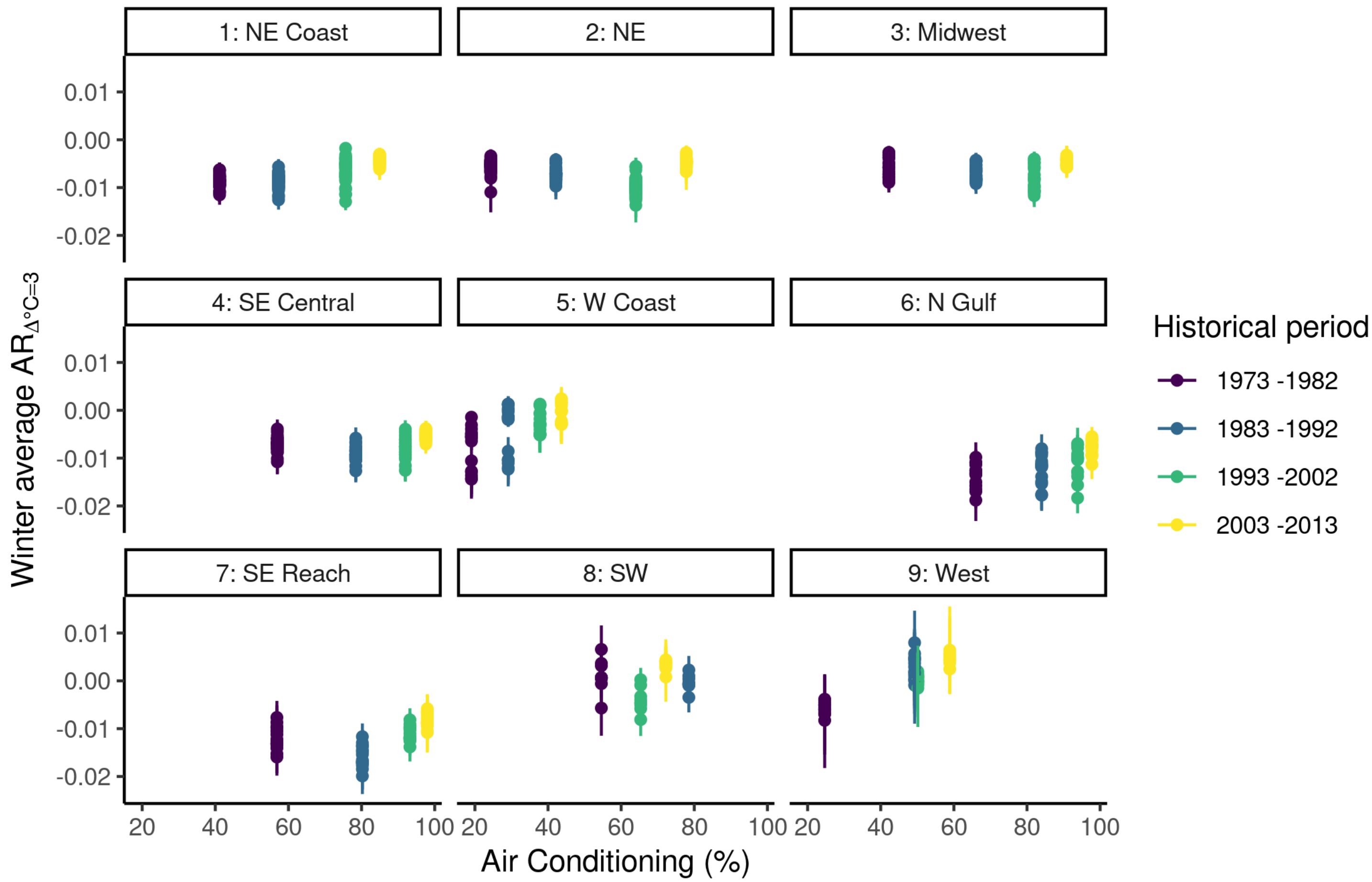


Figure S-8. Differences in attributable mortality at 3°C, shown by the population 65 and over and summer mean temperature in the historical period in which ERFs in the projections were fitted. Although a slight reduction in summer mortality is apparent even as the population over age 65 increases, the causal factor is more likely concurrent changes in air conditioning or other measures that reduce vulnerability.

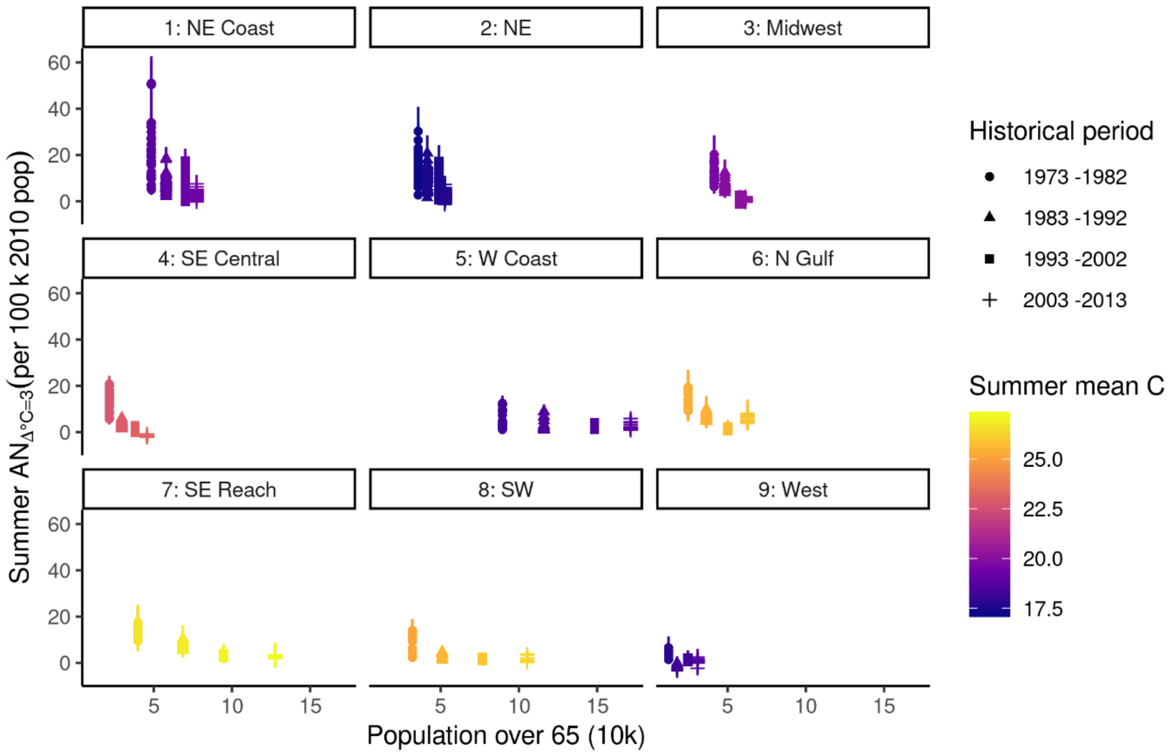


Figure S-9. Projected change in AN at 3°C for each cluster showing the population age 65 or older (per 100,000), and mean winter temperature for the historical period in which the ERFs were fitted.