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Effect of Size/Time Lag Estimation and Determination of Association of Meteorological Factors and Air Pollutants with Fractures

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ABSTRACT

Objective: To determine the association of MFAPs with fracture and to estimate the effect size/time lag.

Design: This was a nationwide population-based study from 2008 to 2017.

Setting: Eight large metropolitan areas in Korea.

Participants: Of 8,093,820 patients with fractures reported in the Korea National Health Insurance database, 2,129,955 were analyzed after the dataset containing the patients' data (age, sex, and site of fractures) were merged with MFAPs. Data on meteorological factors, obtained from the National Climate Data Center of the Korea Meteorological Administration. Additionally, data on air pollutants (atmospheric particulate matter of diameter ≤2.5 μm [$PM_{2.5}$], PM_{10}, ozone, nitrogen dioxide, sulfur dioxide, and carbon monoxide) were obtained from the Air Korea database.

Primary and secondary outcome measures: We hypothesized that there would be the association between MFAPs and the incidence of fracture. A generalized additive model was used while factoring in the nonlinear relationship between MFAPs and fractures as well as a time lag ≤7 days. Multivariate analysis was performed. Backward elimination with an Akaike information criterion was used for fitting the multivariate model.

Results: Overall, in eight urban areas, 2,129,955 patients with fractures were finally analyzed. These included 370,344; 187,370; 173,100; 140,358; 246,775; 6,501; 228,346; 57,183; and 719,978 patients with hip, knee, shoulder, elbow, wrist, hand, ankle, foot, and spine fractures, respectively. Various MFAPs (average temperature, daily rain, wind speed, daily snow, and $PM_{2.5}$)

showed significant association fractures; with positive correlation at time lags 7, 5-7, 5-7, 3-7, and 6-7 days, respectively.

Conclusions: Fractures are affected by various MFAPs. Average temperature, daily rain, wind speed, daily snow, and $PM_{2.5}$ were most closely associated with fracture; thus, improved public awareness are required on these MFAPs for the clinical prevention and management of fractures.

Article summary

Strengths and limitations of this study

- This study's main strength is that the first to investigate the relationship between various MFAPs and fractures, and investigated the interactions between all 13 MFAPs.
- Included 2,129,955 sample size, much larger than majority of other studies.
- The limitations are that study sampled patients who lived in major metroploitan cities and individual MFAPs exposure levels were not evaluated.
- Individual risk factors could not be covered in the analysis.

Keywords: Meteorological factor, air pollution, particulate matter, weather, fracture.

INTRODUCTION

Fractures are common globally, with reported increasing incidence; they are major public health issues, with a heavy burden on health resources.[1-3] The global annual number of fractures is expected to increase due to aging population.[4] In elderly populations, fractures can cause not only temporary dysfunction but also mortality.[2,5] Advances in surgical techniques and postoperative care have led to lower morbidity and mortality; but recently, attention has turned toward the prevention of fractures. Understanding the circumstances surrounding the occurrence of fractures may provide important information about when and why these injuries occur, and may improve fracture prevention.

The relationship between meteorological factors and air pollutants (MFAPs) and their impacts on fracture incidence have been the subject of many studies; most of which reported that more fractures occur during the winter.[6,7] Several hypotheses have been proposed to explain this association; one hypothesis suggest that MFAPs influence fracture incidence through bone metabolism effects. Reduced exposure to ultraviolet radiation may result in reduced vitamin D synthesis, thereby resulting in vitamin D and parathyroid hormone level changes.[8] It affects bone mineral density (BMD) and muscle strength, which can affect mobility and resistance to falls.[9] However, these effects on bone metabolism is long-term impact of MFAPs.[10]

Other hypotheses are based on the short-term relationship of MFAPs with the incidence of fracture. Increased risk of falling depends on the weather conditions due to slippery surfaces.[11] Freezing temperatures, rain, snow, and ice may increase the risk of slipping due to conditions underfoot, and frequent falling is a known risk factor for fractures.[12.13] In low temperatures, there is impaired thermoregulation, hypothermia, and consequent motor coordination deficits that predispose the elderly to falls.[14] Increased risk of falls occurs due to clumsiness in movements.

These can explain many occurrences of fractures, indoors and outdoors.[15] Increased risk of falls can be also due to reduced visual acuity.[16] The presence of haze is associated with increased incidence of fracture. In foggy weather, air pollutants (dust, ash, clay, sand, or ambient air pollutants) are suspended in the atmosphere.[17]

However, most previous studies are focused only on hip fracture or total fractures, without the discrimination of the sites of fractures, specific age groups, and the size and location of hospitals.[10,18,19] There is also insufficient nationwide population-based data. Although previous studies provided information on risk factors of fractures and possible preventive measures for fractures; risk factors, age-specific incidence, and prognoses may differ, depending on the site of fracture. Therefore, it is necessary to determine the association of MFAPs with the occurrence of fractures, by fracture site.[5,20,21]

These hypotheses could help in explaining the results of the association between MFAPs and fracture. Understanding the association between MFAPs and incidence of fracture may lead to improved risk management and the development of appropriate interventions. Thus, this study aimed to determine the association of MFAPs with fracture occurrence, and to estimate their effect size and lag time.

MATERIAL AND METHODS

Data acquisition

It should be mentioned that the study methodology was made based on reference with authors' previous study.[22] The records of patients with fractures were provided by the National Health Insurance Service (NHIS), a government-affiliated agency in Korea. We retrieved the clinical data on bone fractures for both inpatients and outpatients between 2008 and 2017. The sites of bone fractures are as defined in the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) codes with surgical codes: hip (S72.0-S72.3 and S72.7-S72.9); knee (S72.4 and S82.0-S82.2); shoulder (S42.0-S42.3); elbow (S42.4, S52.0-S52.4, and S52.7-S52.9); wrist (S52.5-S52.6); hand (S62 and T10); ankle (S82.3, and S82.5-S82.6); foot (S92, and T12); and spine (S32.0-S32.2, S32.7-S32.8, S22.0-S22.1, and T08). During the study period (2008-2017), we collected 8,093,820 diagnoses of patients with bone fractures and extracted data from the major metropolitan areas, including Seoul, Inchon, Daejeon, Gwangju, Daegu, Ulsan, Busan, and Jeju in Korea. The number of all the patients with fractures in 8 urban areas was 2,129,955 after the dataset containing the patients' data were merged with MFAPs. Data on the general meteorological factors were obtained from the Korea Meteorological Administration National Climate Data Center while those of air pollutants, such as particulate matter, carbon monoxide, and ozone were from Air Korea, during the same period.

Patient and Public Involvement

The study was reviewed and exempted by the Institutional Review Board of Gachon University Gil Medical Center (approval number:GCIRB2019-039), and the requirement to obtain written consent was waived due to the retrospective nature of this study, patients and the public were not involved in the study. All study methods were carried out based on the Declaration of Helsinki.

Statistical analysis

Statistical analyses were conducted in SAS version 9.4 for Windows (SAS Institute, Cary, NC). The results are presented as the relative risk ratio (RR) with 95% confidence intervals (CIs). A *p*-value of less than 0.05 was considered significant.

Models

We performed a time-series analysis that mainly used a generalized additive Poisson regression model (GAM) to control for trends, seasonality, covariates, and the day of the week. Meteorological and air pollutant data were used to calculated the daily average, excluding the outliers in pollution variables on the days when the levels of particulate matter ≤ 2.5 µm in diameter ($PM_{2.5}$) was > 120 µm/m^3. In the time-series analysis, GAM leads to unstable estimates due to autocorrelation between meteorological factors and the sites of bone fractures. Thus, we considered that the time lags until the autocorrelation are 'white noise' which showed 7 days after the sites of the bone fracture occurrences. The sum of autocorrelation terms was included as a covariate in GAM. Moreover, we compared the Akaike Information Criterion (AIC) value among meteorological factors and air pollutants for each candidate model using backward elimination for a better fit of the model. Each fracture site had the lowest AIC value when the model included average temperature (AT), daily rain (DR), wind speed (WS), daily snow (DS), and $PM_{2.5}$.

Our final multivariable model is given as follows;

$$\text{Log}[E(Y)] = \alpha_0 + S(\text{AT}, df = 9) + S(\text{DR}, df = 9) + S(\text{WS}, df = 9) + S(\text{DS}, df = 9) + S(\text{PM}_{2.5}, df = 9) + \textit{offset}\,(\log(\text{province population})) + \gamma\,(\text{day of week}) + \gamma\,(\text{year}) + \sum_{1 \le \theta \le 7} AR_7$$

where Log[E(Y)] is the logged expected number of the daily fracture occurrences, α_0 is the intercept, S is the smooth functions of the meteorological factors using natural cubic splines, *offset* is for the provincial population; γ is the indicator variable for the day of the week and year, while overall autocorrelation effect can be expressed as $AR_1 + \ldots + AR_7$ for 7 lag days.

RESULTS

From a total of 8,093,820 cases of fractures identified during the 10-year study period in 8 urban areas, there were 2,129,955 patients with fractures overall. These included 370,344; 187,370; 173,100; 140,358; 246,775; 6,501; 228,346; 57,183; and 719,978 patients with hip, knee, shoulder, elbow, wrist, hand, ankle, foot, and spine fractures, respectively (Figure 1). Of all the fractures, the spine (33.8%) and hip (17.4%) fractures had the largest proportions. The incidence of fractures increased continuously over the study period. Summaries of the number of fractures by age and sex, and the mean and SDs of MFAPs data, by years of exposure to MFAPs, are presented in Table 1.

Table 1. Baseline characteristics

	2008	**2009**	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**Total**
Fracture	167,501	171,787	196,470	205,022	216,995	225,692	224,339	227,886	240,130	254,133	2,129,955
Male	68,563	68,914	74,383	77,268	79,980	80,561	81,098	81,565	85,014	88,529	785,875
Female	98,938	102,873	122,087	127,754	137,015	145,131	143,241	146,321	155,116	165,604	1,344,080
Age < 20	18,350	17,393	17,202	17,475	17,614	16,915	17,400	16,047	18,545	18,419	175,360
20 - 60	58,315	59,256	66,217	67,717	69,232	71,297	68,321	66,544	67,723	69,005	663,627
> 60	90,836	95,138	113,051	119,830	130,149	137,480	138,618	145,295	153,862	166,709	1,290,968
Site of Fracture											
Hip	28,250	29,029	33,171	34,696	36,931	38,514	39,334	41,453	43,269	45,697	370,344
Male	9,282	9,357	10,571	10,806	11,413	11,596	11,591	11,976	12,445	12,777	111,814
Female	18,968	19,672	22,600	23,890	25,518	26,918	27,743	29,477	30,824	32,920	258,530

Age	< 20	731	614	676	640	605	610	547	462	477	443	5,805
	20 - 60	3,759	3,761	4,169	4,120	4,172	4,255	4,143	4,033	4,044	4,102	40,558
	> 60	23,760	24,654	28,326	29,936	32,154	33,649	34,644	36,958	38,748	41,152	323,981
Knee		16,172	15,974	17,661	18,163	18,690	19,367	19,675	19,619	20,544	21,505	187,370
Male		9,110	8,808	9,488	9,581	9,442	9,362	9,474	9,203	9,325	9,506	93,299
Female		7,062	7,166	8,173	8,582	9,248	10,005	10,201	10,416	11,219	11,999	94,071
Age	< 20	2,185	1,976	2,086	2,036	2,011	2,029	1,917	1,800	2,025	1,924	19,989
	20 - 60	8,170	7,993	8,656	8,710	8,654	8,774	8,602	8,473	8,445	8,625	85,102
	> 60	5,817	6,005	6,919	7,417	8,025	8,564	9,156	9,346	10,074	10,956	82,279
Shoulder		14,218	14,504	15,620	16,200	16,902	17,400	18,188	18,767	20,319	20,982	173,100
Male		8,371	8,529	8,960	9,397	9,769	9,834	10,300	10,480	11,161	11,534	98,335
Female		5,847	5,975	6,660	6,803	7,133	7,566	7,888	8,287	9,158	9,448	74,765
Age	< 20	2,527	2,297	2,385	2,533	2,512	2,317	2,508	2,415	3,130	3,084	25,708
	20 - 60	6,865	7,148	7,536	7,752	8,178	8,486	8,771	8,750	8,992	9,130	81,608
	> 60	4,826	5,059	5,699	5,915	6,212	6,597	6,909	7,602	8,197	8,768	65,784
Elbow		13,879	13,573	13,731	13,701	14,058	14,016	13,895	13,535	14,810	15,160	140,358
Male		7,922	7,611	7,276	7,229	7,503	7,334	7,478	7,185	7,873	7,954	75,365
Female		5,957	5,962	6,455	6,472	6,555	6,682	6,417	6,350	6,937	7,206	64,993
Age	< 20	5,943	5,616	4,959	4,959	5,107	4,960	5,128	4,604	5,612	5,453	52,341
	20 - 60	4,844	4,787	5,235	5,074	5,126	5,186	5,107	5,119	5,129	5,264	50,871
	> 60	3,092	3,170	3,537	3,668	3,825	3,870	3,660	3,812	4,069	4,443	37,146
Wrist		17,494	18,470	23,885	24,686	27,123	28,158	26,065	24,585	26,593	29,716	246,775
Male		6,089	6,306	6,630	6,949	7,186	7,198	7,464	7,145	7,767	8,384	71,118
Female		11,405	12,164	17,255	17,737	19,937	20,960	18,601	17,440	18,826	21,332	175,657
Age	< 20	2,803	2,890	2,684	2,741	2,662	2,445	2,911	2,567	3,163	3,308	28,174

	20 - 60	6,589	6,727	8,661	9,075	9,553	10,151	9,287	8,440	8,967	9,521	86,971
	> 60	8,102	8,853	12,540	12,870	14,908	15,562	13,867	13,578	14,463	16,887	131,630
Hand		507	543	589	624	640	617	732	759	697	793	6,501
Male		423	435	476	504	541	510	600	611	562	637	5,299
Female		84	108	113	120	99	107	132	148	135	156	1,202
Age	< 20	68	64	77	71	83	73	103	118	85	111	853
	20 - 60	399	420	446	482	486	480	549	568	524	557	4,911
	> 60	40	59	66	71	71	64	80	73	88	125	737
Ankle		18,884	19,613	23,044	23,767	24,037	24,862	23,439	23,001	23,210	24,489	228,346
Male		10,107	10,208	11,409	11,888	11,859	11,967	11,299	10,950	10,807	11,335	111,829
Female		8,777	9,405	11,635	11,879	12,178	12,895	12,140	12,051	12,403	13,154	116,517
Age	< 20	2,771	2,669	3,092	3,150	3,295	3,164	3,023	2,981	2,897	2,935	29,977
	20 - 60	11,817	12,305	13,872	14,198	14,179	14,524	13,569	13,046	12,863	13,197	133,570
	> 60	4,296	4,639	6,080	6,419	6,563	7,174	6,847	6,974	7,450	8,357	64,799
Foot		5,293	5,176	5,280	5,494	5,685	5,662	5,877	6,028	6,264	6,424	57,183
Male		3,956	3,759	3,769	3,853	4,075	3,986	4,028	4,019	4,290	4,276	40,011
Female		1,337	1,417	1,511	1,641	1,610	1,676	1,849	2,009	1,974	2,148	17,172
Age	< 20	345	314	274	289	245	250	232	197	195	189	2,530
	20 - 60	3,864	3,703	3,724	3,827	3,924	3,892	3,926	3,881	4,021	3,909	38,671
	> 60	1,084	1,159	1,282	1,378	1,516	1,520	1,719	1,950	2,048	2,326	15,982
Spine		52,804	54,905	63,489	67,691	72,929	77,096	77,134	80,139	84,424	89,367	719,978
Male		13,303	13,901	15,804	17,061	18,192	18,774	18,864	19,996	20,784	22,126	178,805
Female		39,501	41,004	47,685	50,630	54,737	58,322	58,270	60,143	63,640	67,241	541,173
Age	< 20	977	953	969	1,056	1,094	1,067	1,031	903	961	972	9,983
	20 - 60	12,008	12,412	13,918	14,479	14,960	15,549	14,367	14,234	14,738	14,700	141,365

> 60	39,819	41,540	48,602	52,156	56,875	60,480	61,736	65,002	68,725	73,695	568,630
Meteorology (Mean, SD)											
Average Temperature (°C)	13.9(9.6)	13.9(9.4)	13.4(9.6)	12.8(9.4)	12.9(9.8)	13.6(9.6)	14.1(9.6)	14.0(9.4)	14.3(9.2)	14.0(9.3)	
High Temperature (°C)	18.4(9.8)	18.4(9.6)	17.8(9.7)	17.2(9.5)	17.4(9.9)	18.1(9.7)	18.9(9.7)	18.9(9.6)	19.0(9.3)	18.8(9.3)	
Low Temperature (°C)	10.1(9.7)	10.1(9.5)	9.8(10.9)	9.2(10.6)	9.1(11.0)	9.8(9.9)	10.2(9.9)	10.0(9.5)	10.3(9.4)	9.9(9.6)	
Daily Range (°C)	8.3(2.9)	8.3(3.0)	7.9(2.9)	8.0(3.0)	8.3(2.7)	8.2(3.1)	8.6(3.1)	8.8(3.2)	8.7(2.9)	8.8(3.0)	
Vapor Pressure (hPa)	11.9(7.8)	11.7(7.4)	12.5(8.9)	11.4(8.3)	11.3(8.3)	12.3(8.8)	12.9(8.4)	12.3(7.8)	12.9(8.8)	12.3(8.9)	
Solar Radiation (MJ/m^2)	13.5(6.8)	13.8(7.1)	12.9(6.7)	13.1(6.9)	12.8(6.4)	13.0(6.8)	12.9(6.3)	13.1(6.6)	13.2(6.4)	13.7(6.9)	
Sunshine Duration (hr)	12.2(1.7)	12.2(1.7)	12.2(1.7)	12.1(1.7)	12.2(1.7)	12.2(1.7)	12.2(1.7)	12.1(1.7)	12.2(1.7)	12.2(1.7)	
Wind Speed (m/s)	2.4(0.9)	2.5(1.0)	2.5(1.0)	2.6(1.0)	2.7(1.0)	2.7(1.1)	2.5(1.0)	2.6(1.0)	2.4(1.0)	2.3(0.9)	
Daily Rain (mm)	8.8(18.8)	13(31.5)	10(19.9)	12.8(31)	10.8(21)	9.5(18.1)	8.3(16.7)	6.1(10.6)	7.9(16.9)	6.2(16.3)	
Dew Point Temperature (°C)	5.9(11.6)	5.8(11.2)	6.1(12.2)	4.6(12.5)	4.4(12.5)	5.8(12.1)	7.1(11.7)	6.8(10.6)	6.8(12.0)	5.8(12.3)	
Humidity (%)	61(15.2)	61(15.8)	64(15.6)	60(16.9)	59(16.1)	62(16.1)	65(16.9)	65(16.2)	64(16.4)	61(16.1)	
Daily snow (cm)	3.7(3.0)	2.4(2.2)	8.2(6.8)	2.7(2.1)	3.6(2.9)	5.5(4.3)	2.1(1.8)	2.4(2.5)	1.9(2.9)	1.9(1.6)	
Cloud (1/10)	4.7(3.0)	4.6(3.1)	5.1(3.2)	5.0(3.3)	4.9(3.0)	4.8(3.1)	4.8(3.1)	4.8(3.1)	4.8(2.9)	4.6(3.0)	
Air Pollutants (Mean, SD)											
$PM_{2.5}$ (ug/m^3)	-	-	-	-	28(12)	27(13)	25(14)	24(12)	25(14)	23(12)	
PM_{10} (ug/m^3)	56(30)	54(29)	50(28)	49(30)	45(21)	47(23)	48(26)	47(34)	46(19)	45(20)	
O_3 (100ppb)	1.9(0.9)	2.1(1.0)	1.9(0.9)	1.9(1.0)	2.1(1.0)	2.2(1.0)	2.3(1.1)	2.2(1.0)	2.4(1.1)	2.5(1.1)	
NO_2 (100ppb)	3.4(1.4)	3.3(1.3)	3.2(1.3)	3.2(1.3)	3.1(1.2)	3.2(1.3)	3.1(1.3)	3.1(1.3)	2.9(1.1)	2.8(1.1)	
SO_2 (100ppb)	0.6(0.2)	0.5(0.2)	0.5(0.2)	0.5(0.2)	0.5(0.2)	0.5(0.2)	0.5(0.2)	0.5(0.1)	0.4(0.1)	0.4(0.1)	
CO (10ppm)	0.6(0.2)	0.6(0.2)	0.5(0.2)	0.5(0.2)	0.5(0.2)	0.5(0.2)	0.5(0.1)	0.5(0.1)	0.5(0.1)	0.4(0.1)	

O_3 was analyzed by the 8-hour maximum per time or day.

SD denotes standard deviation; min, minimum; max, maximum; ppb, parts-per-billion; ppm, parts-per-million.

Among the 13 MFAPs, AT, DR, WS, DS, and $PM_{2.5}$ had the lowest AIC and were selected for further analyses (Supplemental Table 1). Models including these five selected MFAPs showed statistically significant association with the incidence of fracture.

The predictive models for hip fracture incidence using the univariate GAM are shown in Figure 2. AT showed a typical significant inverted U-shape correlation (*P*< .001), and fracture was higher in both extremes of AT. A negative risk was seen, from -2°C to 21°C, with the highest risk at -7°C. Furthermore, there was an abrupt increase in the risk of hip fracture at extreme temperatures (<-2°C and >21°C). The risk associated with rising DR constantly increased, with a linear correlation, with the incidence of hip fractures (*P*<.001). DR had a negative and positive relative risks at <60 mm and >60 mm, respectively. There was a significant association between hip fracture and WS (*P*<.001), with the highest risk at 1.9 m/s^2. There was a significant association between hip fracture and DS (*P*<.001), with a gradual S-shape curve. Moreover, there was a significant association between hip fracture and $PM_{2.5}$ levels (*P*<.001). An excess risk was seen in the most frequently observed interval (interquartile range [IQR]: 38–64 $\mu g/m^3$).

Fractures at all other sites showed consistent patterns in relation to MFAPs (Supplemental Figure 1-8).

For the five selected variables, time lags were analyzed using multivariate GAM to identify in which prolonged exposure time lag for each variable affects the incidence of fracture (Supplemental Table 2). All the five selected MFAPs showed a maximum lag period of 7 days in the impulse response functions analysis, with no further effect beyond this time point. The box-plot models of the estimated risk for fracture for the five MFAPs are shown in Figure 3.

The multivariate analyses provided the time lags for the effects of the MFAPs on the risk of hip fracture. An increase in AT reflected a significant increase in the risk of hip fracture until 7 days later. The effect of DR, WS, DS, and $PM_{2.5}$ were inversely correlated with the lag time with significantly positive associations, 5–7 days before the occurrence of hip fracture.

The results for the time lags also showed consistent patterns in fractures at all other sites (Supplemental Figure 9-16).

DISCUSSION

In our analysis of the nationwide data of the association between fracture and MFAPs, we found AT, DR, WS, DS, and $PM_{2.5}$ to be closely associated with fracture, among various MFAPs. These selected MFAPs were shown to affect fractures, up to 7 days later. Our evaluation was based on the short-term relationship between the daily variations in different MFAPs and the daily incidence of fractures, which occurred due to the increased risk of falling from adverse MFAPs. This would explain the significantly positive correlations between fractures and several MFAPs. Our study strengthens the importance of the association of various MFAPs in the incidence of fractures. Fractures at all other sites showed a consistent pattern in relation to MFAPs.

Globally, fractures are important public health problems because of the related morbidity and mortality, diminished health-related quality of life, and associated costs. Despite the development of effective surgical treatments, the cost and disabilities following surgery make the prevention of fractures an integral part of any strategy to reduce the impact of fractures, especially with considering the aging trend of the population.[23]

Most fractures are not due to a single cause, but from multiple interactions between individuals and the environment.[24] The reason for the increased number of fractures in adverse MFAPs is not well understood. Recent studies have shown that seasonal patterns observed in fractures may be related to weather patterns such as temperature, snow, or ice.[13.25] However, these previous studies reported associations between fractures and weather data driven by the seasonal factors, not by the daily variability in incidence of fractures. Moreover, analyses of the relationship between fractures and MFAPs using day as the unit of analysis are very rare in the literature.

Several mechanisms have been proposed for the short-term relationship between incidence of fractures and various MFAPs. The mechanisms of fractures in each site appeared to be similar, because fractures at all other sites showed a consistent pattern in relation to MFAPs.

AT, DR, WS, and DS were shown in our study to correlate with a rise in incidence of fractures. Past research has shown that slippery conditions greatly enhance the incidence of fractures, explaining this relationship.[26] DR had a negative relative risk at >60 mm and a relatively positive risk at <60 mm. This can be explained by the fact that when it rains, although people do not go outside; however, with more rain, the road becomes more slippery and traffic accidents increase. DS showed a gradual S-shape curve or irregular pattern due to the few days of snow. Jacobsen et al. associated MFAPs (snow and ice) with the incidence of hip fractures, and observed a significant increase in its incidents, consistent with that of frozen rain.[6] Levy et al. reported a significant increase in the incidence of hip fractures on days with freezing precipitation.[25] Lau et al. concluded that AT is a more important independent risk factor of hip fracture.[27]

We found that AT was closely related to a higher incidence of fractures. A possible mechanism is that weather conditions affect activity levels.[28] Lower temperatures is a cause of blood pressure and hemodynamic changes, and dexterity decreases, leading to increased falls and fractures.[29] It can also reduce physical activity, leading to impaired coordination and consequently bone fragility.[30] The more cold people feel, the more likely they are to wear extra clothes, which may make them clumsier. Darker and colder weather may increase the number of falls.[15] Even though many falls occur indoors, changes in activity levels due to prevailing weather conditions lead to changes in the risk of falls and fracture rates. These provides plausible explanations for why fracture rates are higher on cold days.[28]

Several studies have included the wind as an MFAP variable, in the analysis. One possible explanation could be that the greater the exposure to wind, the greater the risk of falling. Lau et al. found an excessive incidence of hip fractures in more windy days.[27] Mirchandani et al. found a significant correlation between WS and the incidence of hip fractures.[30] Jacobsen et al. observed an increase in the risk of hip fractures with high WS days.[6] Tenias et al. also confirmed increased hip fracture risk with more windy days.[23]

The mechanisms of the relationship between air pollution and incidence of fracture is still unclear. Several studies have investigated the possible relationship between air pollution, BMD, and fractures.[31-33] Alvaer et al. found associations between osteoporosis, forearm fractures, and air pollution. An inverse association was found between BMD and air pollution.[32] Prada et al. found an association between long-term exposure to $PM_{2.5}$ and osteoporosis-related fractures.[34] Chang et al. showed a tendency of increase in association between air pollution and risk of osteoporosis, suggesting that exposure to air pollution could increase the risk of osteoporosis.[31] Therefore, if reduced bone resistance is the mechanism by which air pollution is involved in hip fracture, there would be no effect in the short-term.

What we are actually observing is that air pollution increases the risk of falls.[17] Reduced visual acuity has long been regarded as a risk factor for fracture.[18,35] The reduced hours of sunlight and increased air pollution reduce visual acuity, which predisposes to falls and hip fracture.[16] In a large-scale cohort study, reduced visual acuity increased the likelihood of falls and fractures in the elderly population.[18] Also, acute exposure to $PM_{2.5}$ can stimulate the autonomic nervous system (ANS), increasing the risk of arrhythmia, orthostasis, and syncope.[36] Therefore, $PM_{2.5}$ exposure has been associated with changes in heart rate in the elderly.[37] Reduced heart rate variability due to impairment of ANS could increase the risk of falls.

Our observations on the association of MFAPs with fractures can help in developing the prevention strategies for fractures. The elevated incidence during winter implies that we should raise awareness on the risk of slippery conditions, the importance of keeping warm, improved lighting conditions, and avoiding the wearing of cumbersome clothing.[38]

There were also some limitations in our study. First, we sampled patients who lived in major metropolitan cities. Weather stations are sparsely placed in rural areas, thus we ruled to exclude rural areas owing to the concern of unreliable data. Second, individual MFAPs exposure levels were not evaluated, and we assumed that these individuals were exposed to the identical environment. Therefore, the possibility of ecological fallacy should be noted. Third, individual risk factors such as comorbidities and lifestyle which would affect fracture occurrence could not be covered in the analysis. Fourth, the decision on the occurrence of fracture was only dependent on the diagnostic codes, thus validity of healthcare claims data diagnosis in fracture was debatable. We included only inpatient records to reduce the possibility of coding inaccuracies in our dataset. Painless, undiagnosed, and self-resolved fractures were not included, and there may be a difference between the actual incidence of fracture and the onset of symptoms. Fifth, if citizens tend to stay indoors depending on the level of fine dust, potential bias can be generated during special weather forecasts such as the fine dust warning service. Moreover, discordance between the actual residential areas and weather stations can be found. Finally, the mechanisms underlying the effect of each MFAPs on fracture occurrence could not be identified.

However, our study has several strengths. First, this study was the first to investigate the relationship between various MFAPs and fractures. Second, due to advantage of using national-level data from the NHIS, our study included 2,129,955 sample size, much larger than majority of other studies. As a result of single-payer universal healthcare coverage in Korea, the catchment of fractures was expected to be very high. These facilitated us to analyze a large and credible dataset, which is often hard to implement in other countries. Third, we investigated the interactions between all 13 MFAPs portrayed by the Korean Meteorological Administration, and this allowed a plausible review of the real-world influences and interactions of $PM_{2.5}$ with diverse MFAPs. Fourth, current study covered the capital city and seven other areas in Korea, which could reduce bias by diminishing the region-specific effects such as race, ethnicity, economic levels, and accessibility to hospitals. Fifth, time series Poisson analysis was used with GAM to consider the interaction among MFAPs in terms of fracture occurrence.

CONCLUSIONS

In conclusion, we investigated the relationship between MFAPs and fracture based on healthcare claims and meteorological database. AT, DR, WS, DS, and $PM_{2.5}$ were identified as MFAPs that were most closely associated with fracture. These MFAPs maintained influence for a maximum of 7 days. Visualization of the effect-time association of MFAPs with fracture was possible with in the model. In the future, further confirmatory studies and improved public awareness regarding the MFAPs that are related to the incidence of fracture are needed for the clinical prevention and management of fractures.

Acknowledgements

Ethics approval and consent to participate: The study was reviewed and exempted by the Institutional Review Board of Gachon University Gil Medical Center (approval number:GCIRB2019-039), and the requirement to obtain written consent was waived due to the retrospective nature of this study, patients and the public were not involved in the study. All study methods were carried out based on the Declaration of Helsinki.

Availability of data and materials: The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests: None

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Authors' contributions: Conception and design (T.K., J.J.). Collection and assembly of data (J.H., J.J.). Data analysis and interpretation (T.K., J.H., J.J.). Writing manuscript (M.R., T.K., S.Y.P.) Final approval of manuscript (All authors). Accountable for all aspects of the work (All authors)

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Figure Legends

Figure 1. Flow chart of fracture case selection.

Figure 2. Generalized additive model for the effects of selected meteorological factors on hip fracture incidence. The bold line estimates the relative effect sizes for the hip fracture while the blue area estimates the 95% confidence intervals (Cis). The X-axes represents selected meteorological factors. The Y-axes shows the relative effect sizes for hip fracture. $PM_{2.5}$, particulate matter ≤2.5 μm.

Figure 3. Level of selected meteorological factors and adjusted excess risk for hip fracture: (a) average temperature, (b) daily rain, (c) wind speed, (d) daily snow, and (e) particulate matter ≤2.5 μm ($PM_{2.5}$). The Y-axes show the percentages of adjusted excess risk with 95% confidence intervals (Cis). *p<0.05.

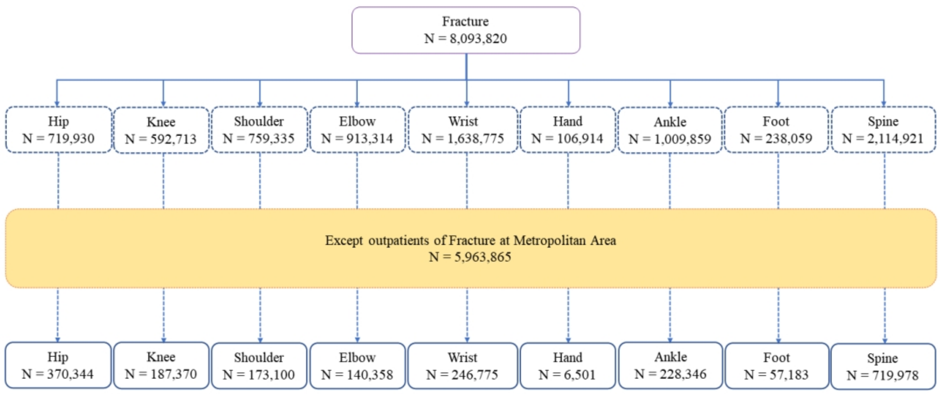

Figure 1. Flow chart of fracture case selection.

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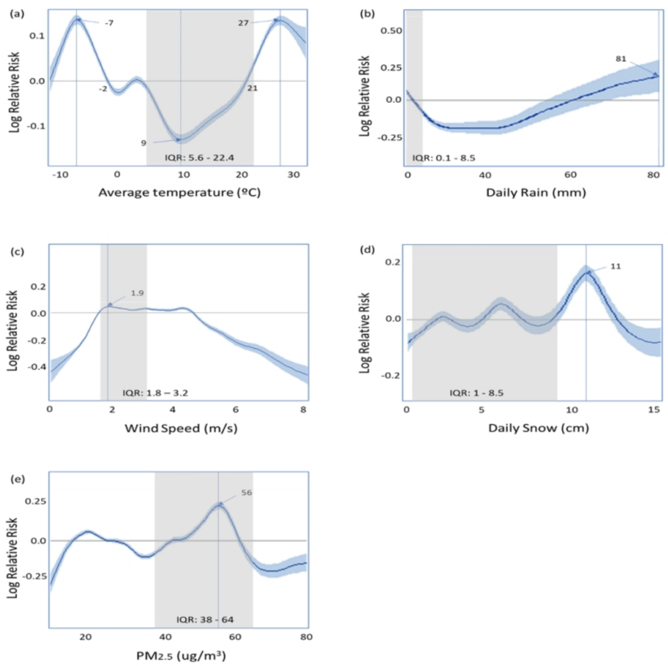

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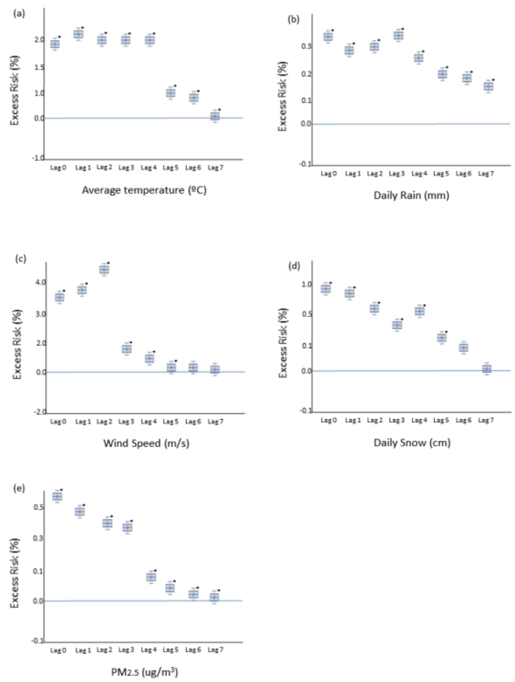

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400x300mm (96 x 96 DPI)

Online supplements

Supplemental Table 1. Akaike Information Criterion (AIC) between site of fracture and meteorological factors including air pollutants (MFAPs)

Supplemental Table 2. Multivariate analysis of GAM with cubic splines for site of fracture depending on lags through from 2008 to 2017

Supplemental Figure 1. Generalized additive model for the effects of selected meteorological factors on the incidence of knee fracture

Supplemental Figure 2. Generalized additive model for the effects of selected meteorological factors on the incidence of shoulder fracture

Supplemental Figure 3. Generalized additive model for the effects of selected meteorological factors on the incidence of elbow fracture

Supplemental Figure 4. Generalized additive model for the effects of selected meteorological factors on the incidence of wrist fracture

Supplemental Figure 5. Generalized additive model for the effects of selected meteorological factors on the incidence of hand fracture

Supplemental Figure 6. Generalized additive model for the effects of selected meteorological factors on the incidence of ankle fracture

Supplemental Figure 7. Generalized additive model for the effects of selected meteorological factors on the incidence of foot fracture

Supplemental Figure 8. Generalized additive model for the effects of selected meteorological factors on the incidence of spine fracture

Supplemental Figure 9. Levels of the selected meteorological factors and adjusted excess risks of the knee fracture

Supplemental Figure 10. Levels of the selected meteorological factors and adjusted excess risks of the shoulder fracture

Supplemental Figure 11. Levels of the selected meteorological factors and adjusted excess risks of the elbow fracture

Supplemental Figure 12. Levels of the selected meteorological factors and adjusted excess risks of the wrist fracture

Supplemental Figure 13. Levels of the selected meteorological factors and adjusted excess risks of the hand fracture

Supplemental Figure 14. Levels of the selected meteorological factors and adjusted excess risks of the ankle fracture

Supplemental Figure 15. Levels of the selected meteorological factors and adjusted excess risks of the foot fracture

Supplemental Figure 16. Levels of the selected meteorological factors and adjusted excess risks of the spine fracture

Supplemental Table 1.

Akaike Information Criterion (AIC) between site of fracture and meteorological factors including air pollutants (MFAPs)

Test	MFAP as effect	AIC
Hip		
1	Average Temperature, Diurnal Temperature Range, Daily Rain, Wind Speed, Dew point Temperature, Humidity, Vapor Pressure, Sunshine Duration, Solar Radiation, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, SO_2, O_3, NO_2	197.3
2	Average Temperature, Diurnal Temperature Range, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Sunshine Duration, Solar Radiation, Daily Snow, PM_{10}, $PM_{2.5}$, CO, O_3, NO_2	196.7
3	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Sunshine Duration, Solar Radiation, Daily Snow, PM_{10}, $PM_{2.5}$, CO, NO_2	196.2
4	Average Temperature, Daily Rain, Wind Speed, Vapor Pressure, Sunshine Duration, Solar Radiation, Daily Snow, PM_{10}, $PM_{2.5}$, CO,NO_2	191.7
5	Average Temperature, Daily Rain, Wind Speed, Vapor Pressure, Daily Snow, PM_{10}, $PM_{2.5}$, CO, NO_2	189.6
6	Average Temperature, Daily Rain, Wind Speed, Vapor Pressure, Daily Snow, PM_{10}, $PM_{2.5}$	188.5
7	Average Temperature, Daily Rain, Wind Speed, Daily Snow, PM_{10}, $PM_{2.5}$	188.5
8	**Average Temperature, Daily Rain, Wind Speed, Daily Snow, $PM_{2.5}$**	**187.3**
Knee		
Test	MFAP as effect	AIC
1	Average Temperature, Diurnal Temperature Range, Daily Rain, Wind Speed, Dew point Temperature, Humidity, Vapor Pressure, Sunshine Duration, Solar Radiation, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, SO_2, O_3, NO_2	125.8
2	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Sunshine Duration, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, SO_2, O_3, NO_2	123.6
3	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Sunshine Duration, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, NO_2	123.1
4	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO	123.1
5	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Daily Snow, $PM_{2.5}$, CO	121.7
6	Average Temperature, Daily Rain, Wind Speed, Humidity, Daily Snow, $PM_{2.5}$, CO	121.7
7	**Average Temperature, Daily Rain, Wind Speed, Daily Snow, $PM_{2.5}$**	**119.5**
Shoulder		
Test	MFAP as effect	AIC
1	Average Temperature, Diurnal Temperature Range, Daily Rain, Wind Speed, Dew point Temperature, Humidity, Vapor Pressure, Sunshine	151.1

	Duration, Solar Radiation, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, SO_2, O_3, NO_2	
2	Average Temperature, Diurnal Temperature Range, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Sunshine Duration, Solar Radiation, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, NO_2	149.9
3	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Sunshine Duration, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, NO_2	146.6
4	Average Temperature, Daily Rain, Wind Speed, Humidity, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, NO_2	146.3
5	Average Temperature, Daily Rain, Wind Speed, Humidity, Daily Snow, PM_{10}, $PM_{2.5}$	146.2
6	**Average Temperature, Daily Rain, Wind Speed, Daily Snow, $PM_{2.5}$**	**142.8**
	Elbow	
Test	MFAP as effect	AIC
1	Average Temperature, Diurnal Temperature Range, Daily Rain, Wind Speed, Dew point Temperature, Humidity, Vapor Pressure, Sunshine Duration, Solar Radiation, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, SO_2, O_3, NO_2	153.7
2	Average Temperature, Diurnal Temperature Range, Daily Rain, Wind Speed, Dew point Temperature, Vapor Pressure, Sunshine Duration, Solar Radiation, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, NO_2	153.5
3	Average Temperature, Daily Rain, Wind Speed, Dew point Temperature, Vapor Pressure, Sunshine Duration, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, NO_2	149.1
4	Average Temperature, Daily Rain, Wind Speed, Dew point Temperature, Vapor Pressure, Daily Snow, PM_{10}, $PM_{2.5}$, NO_2	148.2
5	Average Temperature, Daily Rain, Wind Speed, Daily Snow, PM_{10}, $PM_{2.5}$	148.1
6	**Average Temperature, Daily Rain, Wind Speed, Daily Snow, $PM_{2.5}$**	**145.8**
	Wrist	
Test	MFAP as effect	AIC
1	Average Temperature, Diurnal Temperature Range, Daily Rain, Wind Speed, Dew point Temperature, Humidity, Vapor Pressure, Sunshine Duration, Solar Radiation, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, SO_2, O_3, NO_2	480.2
2	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Sunshine Duration, Solar Radiation, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, O_3, NO_2	480.1
3	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Sunshine Duration, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO	477.8
4	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Daily Snow, PM_{10}, $PM_{2.5}$	473.4
5	Average Temperature, Daily Rain, Wind Speed, Daily Snow, PM_{10}, $PM_{2.5}$	469.6
6	**Average Temperature, Daily Rain, Wind Speed, Daily Snow, $PM_{2.5}$**	**460.5**
	Hand	
Test	MFAP as effect	AIC

1	Average Temperature, Diurnal Temperature Range, Daily Rain, Wind Speed, Dew point Temperature, Humidity, Vapor Pressure, Sunshine Duration, Solar Radiation, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, SO_2, O_3, NO_2	1531.9
2	Average Temperature, Daily Rain, Wind Speed, Vapor Pressure, Sunshine Duration, Solar Radiation, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, SO_2, O_3, NO_2	1467.8
3	Average Temperature, Daily Rain, Wind Speed, Sunshine Duration, Solar Radiation, Daily Snow, Cloud, $PM_{2.5}$, CO, O_3, NO_2	1465.1
4	Average Temperature, Daily Rain, Wind Speed, Sunshine Duration, Daily Snow, $PM_{2.5}$, CO, NO_2	1455.3
5	Average Temperature, Daily Rain, Wind Speed, Daily Snow, $PM_{2.5}$, NO_2	1458.1
6	**Average Temperature, Daily Rain, Wind Speed, Daily Snow, $PM_{2.5}$**	**1452.4**
	Ankle	
Test	MFAP as effect	AIC
1	Average Temperature, Diurnal Temperature Range, Daily Rain, Wind Speed, Dew point Temperature, Humidity, Vapor Pressure, Sunshine Duration, Solar Radiation, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, SO_2, O_3, NO_2	237.1
2	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Sunshine Duration, Solar Radiation, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, SO_2, NO_2	235.7
3	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Sunshine Duration, Daily Snow, Cloud, $PM_{2.5}$, CO, NO_2	231.2
4	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Daily Snow, $PM_{2.5}$, NO_2	230.3
5	Average Temperature, Daily Rain, Wind Speed, Humidity, Daily Snow, $PM_{2.5}$	230.2
6	**Average Temperature, Daily Rain, Wind Speed, Daily Snow, $PM_{2.5}$**	**229.6**
	Foot	
Test	MFAP as effect	AIC
1	Average Temperature, Diurnal Temperature Range, Daily Rain, Wind Speed, Dew point Temperature, Humidity, Vapor Pressure, Sunshine Duration, Solar Radiation, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, SO_2, O_3, NO_2	299.2
2	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Sunshine Duration, Solar Radiation, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, SO_2, O_3, NO_2	290.8
3	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Sunshine Duration, Daily Snow, Cloud, $PM_{2.5}$, CO, SO_2, O_3, NO_2	290.5
4	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Sunshine Duration, Daily Snow, Cloud, $PM_{2.5}$, CO, NO_2	290.3
5	Average Temperature, Daily Rain, Wind Speed, Humidity, Daily Snow, Cloud, $PM_{2.5}$, CO, NO_2	289.8
6	Average Temperature, Daily Rain, Wind Speed, Daily Snow, $PM_{2.5}$, CO, NO_2	289.6
7	**Average Temperature, Daily Rain, Wind Speed, Daily Snow, $PM_{2.5}$**	**289.1**
	Spine	

Test	MFAP as effect	AIC
1	Average Temperature, Diurnal Temperature Range, Daily Rain, Wind Speed, Dew point Temperature, Humidity, Vapor Pressure, Sunshine Duration, Solar Radiation, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, SO_2, O_3, NO_2	434.1
2	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Sunshine Duration, Solar Radiation, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, SO_2, O_3, NO_2	429.2
3	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Sunshine Duration, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, SO_2, NO_2	425.6
4	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Sunshine Duration, Daily Snow, PM_{10}, $PM_{2.5}$, CO, NO_2	425.1
5	Average Temperature, Daily Rain, Wind Speed, Humidity, Daily Snow, PM_{10}, $PM_{2.5}$, CO, NO_2	424.7
6	Average Temperature, Daily Rain, Wind Speed, Humidity, Daily Snow, $PM_{2.5}$, CO	424.5
7	**Average Temperature, Daily Rain, Wind Speed, Humidity, Daily Snow, $PM_{2.5}$**	**422.1**

Supplemental Table 2.

Multivariate analysis of GAM with cubic splines for site of fracture depending on lags through from 2008 to 2017

Time	Variables	Hip				Knee			
		RR	ER(%)	95% CI	P-value	RR	ER(%)	95% CI	P-value
Lag 0	Avg. Temp.	1.0199	1.99	[1.0196-1.0202]	<.0001	1.0162	1.62	[1.0159-1.0165]	<.0001
	Daily Rain	1.0033	0.33	[1.0030-1.0036]	<.0001	1.0021	0.21	[1.0018-1.0024]	<.0001
	Wind Speed	1.0354	3.54	[1.0324-1.0383]	<.0001	1.0242	2.42	[1.0210-1.0275]	<.0001
	Daily Snow	1.0099	0.99	[1.0081-1.0117]	<.0001	1.0116	1.16	[1.0097-1.0135]	<.0001
	$PM_{2.5}$	1.0055	0.55	[1.0052-1.0057]	<.0001	1.0037	0.37	[1.0034-1.0040]	<.0001
Lag 1	Avg. Temp.	1.0202	2.02	[1.0199-1.0204]	<.0001	1.0163	1.63	[1.0161-1.0166]	<.0001
	Daily Rain	1.0029	0.29	[1.0027-1.0031]	<.0001	1.0015	0.15	[1.0013-1.0017]	<.0001
	Wind Speed	1.0379	3.79	[1.0359-1.0399]	<.0001	1.0298	2.98	[1.0274-1.0323]	<.0001
	Daily Snow	1.0083	0.83	[1.0070-1.0096]	0.0003	1.0115	1.15	[1.0100-1.0129]	<.0001
	$PM_{2.5}$	1.0048	0.48	[1.0046-1.0050]	<.0001	1.0037	0.37	[1.0035-1.0040]	<.0001
Lag 2	Avg. Temp.	1.0200	2.00	[1.0198-1.0203]	<.0001	1.0163	1.63	[1.0161-1.0166]	<.0001
	Daily Rain	1.0030	0.30	[1.0028-1.0032]	0.0002	1.0017	0.17	[1.0015-1.0019]	<.0001
	Wind Speed	1.0442	4.42	[1.0422-1.0462]	<.0001	1.0343	3.43	[1.0319-1.0367]	<.0001
	Daily Snow	1.0058	0.58	[1.0045-1.0071]	<.0001	1.0099	0.99	[1.0085-1.0114]	<.0001
	$PM_{2.5}$	1.0039	0.39	[1.0037-1.0041]	<.0001	1.0029	0.29	[1.0027-1.0032]	0.0005
Lag 3	Avg. Temp.	1.0200	2.00	[1.0198-1.0202]	<.0001	1.0163	1.63	[1.0161-1.0165]	<.0001
	Daily Rain	1.0034	0.34	[1.0032-1.0036]	0.0001	1.0018	0.18	[1.0015-1.0020]	0.0002
	Wind Speed	1.0180	1.80	[1.0158-1.0201]	<.0001	1.0286	2.86	[1.0262-1.0310]	<.0001
	Daily Snow	1.0036	0.36	[1.0023-1.0050]	0.0004	1.0058	0.58	[1.0043-1.0074]	<.0001
	$PM_{2.5}$	1.0034	0.34	[1.0032-1.0037]	<.0001	1.0031	0.31	[1.0028-1.0034]	<.0001
Lag 4	Avg. Temp.	1.0200	2.00	[1.0198-1.0202]	<.0001	1.0162	1.62	[1.0159-1.0164]	<.0001
	Daily Rain	1.0026	0.26	[1.0024-1.0028]	0.0002	1.0020	0.20	[1.0017-1.0022]	0.0005
	Wind Speed	1.0096	0.96	[1.0075-1.0118]	<.0001	1.0229	2.29	[1.0204-1.0254]	<.0001
	Daily Snow	1.0052	0.52	[1.0039-1.0066]	<.0001	1.0026	0.26	[1.0010-1.0042]	<.0001
	$PM_{2.5}$	1.0009	0.09	[1.0007-1.0012]	0.0512	1.0024	0.24	[1.0021-1.0026]	<.0001
Lag 5	Avg. Temp.	1.0101	1.01	[1.0099-1.0103]	<.0001	1.0163	1.63	[1.0161-1.0165]	<.0001

	Daily Rain	1.0020	0.20	[1.0018-1.0022]	0.0001	1.0017	0.17	[1.0015-1.0020]	<.0001
	Wind Speed	1.0023	0.23	[1.0001-1.0044]	0.0432	1.0204	2.04	[1.0179-1.0229]	<.0001
	Daily Snow	1.0018	0.18	[1.0003-1.0032]	<.0001	1.0024	0.24	[1.0007-1.0041]	0.0218
	$PM_{2.5}$	1.0006	0.06	[1.0003-1.0008]	<.0001	1.0019	0.19	[1.0017-1.0022]	<.0001
Lag 6	Avg. Temp.	1.0099	0.99	[1.0097-1.0101]	<.0001	1.0163	1.63	[1.0160-1.0165]	<.0001
	Daily Rain	1.0019	0.19	[1.0017-1.0021]	0.0002	1.0016	0.16	[1.0014-1.0018]	<.0001
	Wind Speed	1.0020	0.20	[0.9998-1.0041]	0.4289	1.0103	1.03	[1.0079-1.0128]	<.0001
	Daily Snow	1.0011	0.11	[0.9996-1.0025]	0.5743	1.0007	0.07	[0.9990-1.0023]	0.1976
	$PM_{2.5}$	1.0004	0.04	[1.0002-1.0006]	0.0012	1.0014	0.14	[1.0011-1.0017]	<.0001
Lag 7	Avg. Temp.	1.0020	0.20	[1.0018-1.0022]	0.0023	1.0163	1.63	[1.0161-1.0165]	<.0001
	Daily Rain	1.0016	0.16	[1.0014-1.0018]	0.0005	1.0009	0.09	[1.0006-1.0011]	0.0356
	Wind Speed	1.0014	0.14	[0.9993-1.0034]	0.4980	1.0024	0.24	[0.9999-1.0048]	0.5569
	Daily Snow	1.0009	0.09	[0.9995-1.0023]	0.5533	1.0003	0.03	[0.9988-1.0019]	0.7635
	$PM_{2.5}$	1.0003	0.03	[1.0001-1.0005]	0.0045	1.0009	0.09	[1.0006-1.0012]	0.0144

Time	Variables	Shoulder				Elbow			
		RR	ER(%)	95% CI	P-value	RR	ER(%)	95% CI	P-value
Lag 0	Avg. Temp.	1.0134	1.34	[1.0131-1.0137]	<.0001	1.0101	1.01	[1.0099-1.0104]	<.0001
	Daily Rain	1.0015	0.15	[1.0012-1.0018]	<.0001	1.0015	0.15	[1.0012-1.0018]	<.0001
	Wind Speed	1.0165	1.65	[1.0134-1.0197]	<.0001	1.0124	1.24	[1.0093-1.0155]	<.0001
	Daily Snow	1.0128	1.28	[1.0110-1.0146]	<.0001	1.0149	1.49	[1.0132-1.0166]	<.0001
	$PM_{2.5}$	1.0032	0.32	[1.0029-1.0035]	<.0001	1.0019	0.19	[1.0016-1.0023]	<.0001
Lag 1	Avg. Temp.	1.0136	1.36	[1.0134-1.0138]	<.0001	1.0103	1.03	[1.0101-1.0105]	<.0001
	Daily Rain	1.0013	0.13	[1.0012-1.0015]	<.0001	1.0008	0.08	[1.0006-1.0010]	0.0013
	Wind Speed	1.0209	2.09	[1.0189-1.0230]	<.0001	1.0178	1.78	[1.0159-1.0196]	<.0001
	Daily Snow	1.0130	1.30	[1.0118-1.0142]	<.0001	1.0144	1.44	[1.0134-1.0155]	<.0001
	$PM_{2.5}$	1.0033	0.33	[1.0031-1.0035]	<.0001	1.0020	0.20	[1.0018-1.0022]	<.0001
Lag 2	Avg. Temp.	1.0135	1.35	[1.0133-1.0137]	<.0001	1.0104	1.04	[1.0102-1.0105]	<.0001
	Daily Rain	1.0014	0.14	[1.0012-1.0016]	<.0001	1.0008	0.08	[1.0006-1.0009]	0.0017
	Wind Speed	1.0255	2.55	[1.0234-1.0275]	<.0001	1.0201	2.01	[1.0182-1.0219]	<.0001
	Daily Snow	1.0112	1.12	[1.0099-1.0124]	<.0001	1.0116	1.16	[1.0105-1.0126]	<.0001

	$PM_{2.5}$	1.0034	0.34	[1.0031-1.0036]	<.0001	1.0021	0.21	[1.0019-1.0023]	0.0005
Lag 3	Avg. Temp.	1.0135	1.35	[1.0133-1.0137]	<.0001	1.0103	1.03	[1.0101-1.0105]	<.0001
	Daily Rain	1.0012	0.12	[1.0010-1.0013]	0.0006	1.0009	0.09	[1.0007-1.0010]	0.0018
	Wind Speed	1.0218	2.18	[1.0198-1.0239]	<.0001	1.0248	2.48	[1.0230-1.0266]	<.0001
	Daily Snow	1.0075	0.75	[1.0062-1.0088]	<.0001	1.0097	0.97	[1.0086-1.0108]	<.0001
	$PM_{2.5}$	1.0033	0.33	[1.0030-1.0035]	<.0001	1.0019	0.19	[1.0017-1.0021]	<.0001
Lag 4	Avg. Temp.	1.0135	1.35	[1.0133-1.0137]	<.0001	1.0101	1.01	[1.0099-1.0103]	<.0001
	Daily Rain	1.0014	0.14	[1.0012-1.0016]	<.0001	1.0010	0.10	[1.0009-1.0012]	<.0001
	Wind Speed	1.0181	1.81	[1.0160-1.0201]	<.0001	1.0188	1.88	[1.0170-1.0207]	<.0001
	Daily Snow	1.0028	0.28	[1.0015-1.0042]	<.0001	1.0070	0.70	[1.0059-1.0082]	<.0001
	$PM_{2.5}$	1.0023	0.23	[1.0021-1.0026]	<.0001	1.0017	0.17	[1.0015-1.0019]	<.0001
Lag 5	Avg. Temp.	1.0137	1.37	[1.0135-1.0138]	<.0001	1.0102	1.02	[1.0101-1.0104]	<.0001
	Daily Rain	1.0014	0.14	[1.0012-1.0015]	0.0001	1.0009	0.09	[1.0007-1.0010]	0.0011
	Wind Speed	1.0173	1.73	[1.0152-1.0194]	<.0001	1.0172	1.72	[1.0153-1.0190]	<.0001
	Daily Snow	1.0002	0.02	[0.9988-1.0017]	0.1489	1.0013	0.13	[1.0000-1.0025]	0.0561
	$PM_{2.5}$	1.0017	0.17	[1.0015-1.0020]	<.0001	1.0010	0.10	[1.0008-1.0013]	0.0023
Lag 6	Avg. Temp.	1.0136	1.36	[1.0134-1.0138]	<.0001	1.0103	1.03	[1.0101-1.0105]	<.0001
	Daily Rain	1.0008	0.08	[1.0007-1.0010]	0.0028	1.0009	0.09	[1.0007-1.0010]	0.0013
	Wind Speed	1.0149	1.49	[1.0129-1.0170]	<.0001	1.0153	1.53	[1.0135-1.0171]	<.0001
	Daily Snow	1.0001	0.01	[0.9987-1.0015]	0.5731	1.0012	0.12	[0.9999-1.0024]	0.4791
	$PM_{2.5}$	1.0012	0.12	[1.0010-1.0015]	0.0010	1.0009	0.09	[1.0007-1.0011]	0.0031
Lag 7	Avg. Temp.	1.0137	1.37	[1.0135-1.0139]	<.0001	1.0103	1.03	[1.0102-1.0105]	<.0001
	Daily Rain	1.0001	0.01	[1.0000-1.0003]	0.0556	1.0007	0.07	[1.0005-1.0008]	0.0033
	Wind Speed	1.0111	1.11	[1.0090-1.0131]	<.0001	1.0119	1.19	[1.0100-1.0137]	0.5569
	Daily Snow	1.0001	0.01	[0.9988-1.0015]	0.7631	1.0009	0.09	[0.9997-1.0021]	0.6583
	$PM_{2.5}$	1.0003	0.03	[1.0000-1.0005]	0.0612	1.0008	0.08	[1.0006-1.0010]	0.0237

Time	Variables	Wrist				Hand			
		RR	ER(%)	95% CI	P-value	RR	ER(%)	95% CI	P-value
Lag 0	Avg. Temp.	1.0148	1.48	[1.0146-1.0151]	<.0001	1.0203	2.03	[1.0195-1.0211]	<.0001
	Daily Rain	1.0023	0.23	[1.0020-1.0025]	<.0001	1.0025	0.25	[1.0016-1.0033]	<.0001

	Wind Speed	1.0174	1.74	[1.0147-1.0201]	<.0001	1.0058	0.58	[0.9959-1.0157]	<.0001
	Daily Snow	1.0145	1.45	[1.0133-1.0158]	<.0001	1.0241	2.41	[1.0196-1.0285]	<.0001
	$PM_{2.5}$	1.0020	0.20	[1.0017-1.0023]	<.0001	1.0047	0.47	[1.0038-1.0056]	<.0001
Lag 1	Avg. Temp.	1.0149	1.49	[1.0148-1.0150]	<.0001	1.0205	2.05	[1.0196-1.0213]	<.0001
	Daily Rain	1.0020	0.20	[1.0019-1.0022]	<.0001	1.0027	0.27	[1.0019-1.0035]	0.0013
	Wind Speed	1.0218	2.18	[1.0206-1.0230]	<.0001	1.0157	1.57	[1.0061-1.0254]	<.0001
	Daily Snow	1.0143	1.43	[1.0137-1.0148]	<.0001	1.0237	2.37	[1.0188-1.0285]	<.0001
	$PM_{2.5}$	1.0022	0.22	[1.0020-1.0023]	<.0001	1.0043	0.43	[1.0033-1.0052]	<.0001
Lag 2	Avg. Temp.	1.0149	1.49	[1.0148-1.0151]	<.0001	1.0207	2.07	[1.0198-1.0215]	<.0001
	Daily Rain	1.0020	0.20	[1.0019-1.0021]	<.0001	1.0014	0.14	[1.0006-1.0021]	0.0024
	Wind Speed	1.0238	2.38	[1.0226-1.0250]	<.0001	1.0237	2.37	[1.0141-1.0332]	<.0001
	Daily Snow	1.0116	1.16	[1.0110-1.0122]	<.0001	1.0172	1.72	[1.0122-1.0223]	<.0001
	$PM_{2.5}$	1.0021	0.21	[1.0019-1.0022]	<.0001	1.0041	0.41	[1.0031-1.0050]	<.0001
Lag 3	Avg. Temp.	1.0149	1.49	[1.0147-1.0150]	<.0001	1.0207	2.07	[1.0199-1.0215]	<.0001
	Daily Rain	1.0018	0.18	[1.0017-1.0019]	<.0001	1.0019	0.19	[1.0012-1.0027]	<.0001
	Wind Speed	1.0282	2.82	[1.0270-1.0293]	<.0001	1.0308	3.08	[1.0214-1.0402]	<.0001
	Daily Snow	1.0099	0.99	[1.0093-1.0105]	<.0001	1.0112	1.12	[1.0060-1.0165]	<.0001
	$PM_{2.5}$	1.0025	0.25	[1.0023-1.0026]	<.0001	1.0049	0.49	[1.0039-1.0058]	<.0001
Lag 4	Avg. Temp.	1.0146	1.46	[1.0145-1.0147]	<.0001	1.0205	2.05	[1.0197-1.0213]	<.0001
	Daily Rain	1.0019	0.19	[1.0018-1.0020]	<.0001	1.0032	0.32	[1.0023-1.0041]	<.0001
	Wind Speed	1.0197	1.97	[1.0185-1.0209]	<.0001	1.0335	3.35	[1.0240-1.0430]	<.0001
	Daily Snow	1.0078	0.78	[1.0071-1.0084]	<.0001	1.0083	0.83	[1.0031-1.0135]	<.0001
	$PM_{2.5}$	1.0025	0.25	[1.0023-1.0026]	<.0001	1.0039	0.39	[1.0030-1.0049]	<.0001
Lag 5	Avg. Temp.	1.0146	1.46	[1.0145-1.0147]	<.0001	1.0205	2.05	[1.0197-1.0213]	<.0001
	Daily Rain	1.0017	0.17	[1.0015-1.0018]	<.0001	1.0022	0.22	[1.0015-1.0030]	<.0001
	Wind Speed	1.0173	1.73	[1.0161-1.0185]	<.0001	1.0340	3.40	[1.0245-1.0434]	<.0001
	Daily Snow	1.0030	0.30	[1.0024-1.0037]	<.0001	1.0017	0.17	[0.9961-1.0073]	0.1469
	$PM_{2.5}$	1.0012	0.12	[1.0011-1.0014]	<.0001	1.0021	0.21	[1.0010-1.0031]	<.0001
Lag 6	Avg. Temp.	1.0146	1.46	[1.0145-1.0147]	<.0001	1.0206	2.06	[1.0198-1.0215]	<.0001
	Daily Rain	1.0014	0.14	[1.0013-1.0015]	<.0001	1.0006	0.06	[0.9999-1.0012]	0.8631
	Wind Speed	1.0124	1.24	[1.0112-1.0136]	<.0001	1.0184	1.84	[1.0090-1.0278]	<.0001

	Daily Snow	1.0026	0.26	[1.0020-1.0033]	<.0001	1.0010	0.10	[0.9954-1.0066]	0.7764
	$PM_{2.5}$	1.0010	0.10	[1.0009-1.0012]	0.0009	1.0012	0.12	[1.0002-1.0022]	0.0035
Lag 7	Avg. Temp.	1.0146	1.46	[1.0145-1.0147]	<.0001	1.0205	2.05	[1.0197-1.0214]	<.0001
	Daily Rain	1.0009	0.09	[1.0007-1.0010]	0.0004	1.0002	0.02	[0.9994-1.0011]	0.7490
	Wind Speed	1.0106	1.06	[1.0094-1.0118]	<.0001	1.0024	0.24	[0.9929-1.0118]	0.6931
	Daily Snow	1.0014	0.14	[1.0007-1.0020]	0.0012	1.0003	0.03	[0.9949-1.0057]	0.6132
	$PM_{2.5}$	1.0008	0.08	[1.0007-1.0010]	0.0011	1.0008	0.08	[0.9998-1.0018]	0.3885

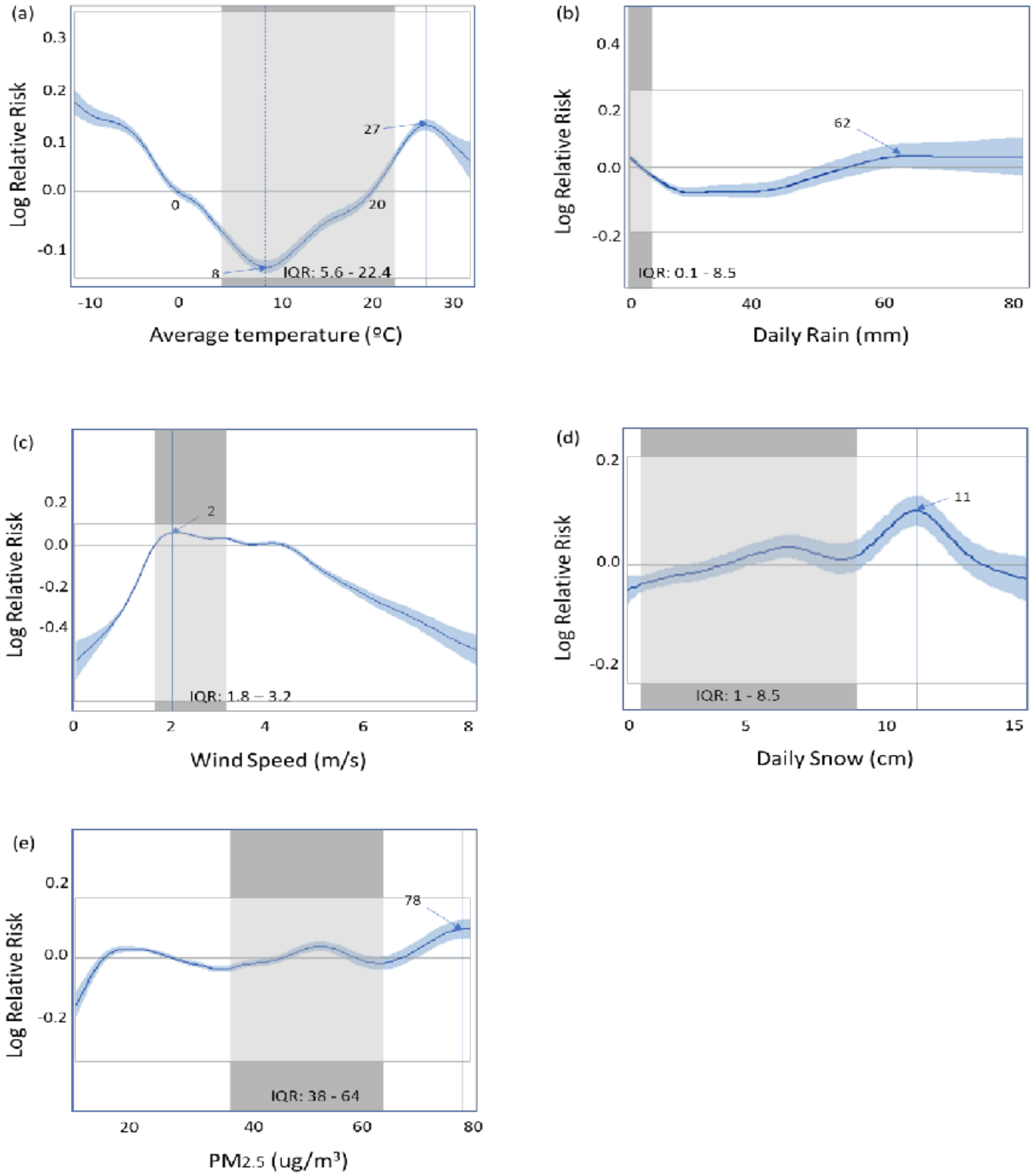
Time	Variables	Ankle				Foot			
		RR	ER(%)	95% CI	P-value	RR	ER(%)	95% CI	P-value
Lag 0	Avg. Temp.	1.0144	1.44	[1.0141-1.0146]	<.0001	1.0122	1.22	[1.0117-1.0126]	<.0001
	Daily Rain	1.0018	0.18	[1.0015-1.0021]	<.0001	1.0020	0.20	[1.0015-1.0025]	<.0001
	Wind Speed	1.0210	2.10	[1.0181-1.0239]	<.0001	1.0265	2.65	[1.0215-1.0315]	<.0001
	Daily Snow	1.0115	1.15	[1.0100-1.0131]	<.0001	1.0197	1.97	[1.0166-1.0228]	<.0001
	$PM_{2.5}$	1.0026	0.26	[1.0023-1.0029]	<.0001	1.0041	0.41	[1.0036-1.0046]	<.0001
Lag 1	Avg. Temp.	1.0144	1.44	[1.0143-1.0146]	<.0001	1.0122	1.22	[1.0118-1.0127]	<.0001
	Daily Rain	1.0015	0.15	[1.0013-1.0016]	<.0001	1.0009	0.09	[1.0004-1.0013]	0.0022
	Wind Speed	1.0257	2.57	[1.0241-1.0273]	<.0001	1.0358	3.58	[1.0309-1.0407]	<.0001
	Daily Snow	1.0119	1.19	[1.0110-1.0128]	<.0001	1.0199	1.99	[1.0168-1.0229]	<.0001
	$PM_{2.5}$	1.0027	0.27	[1.0026-1.0029]	<.0001	1.0044	0.44	[1.0039-1.0049]	<.0001
Lag 2	Avg. Temp.	1.0144	1.44	[1.0143-1.0146]	<.0001	1.0123	1.23	[1.0118-1.0127]	<.0001
	Daily Rain	1.0017	0.17	[1.0016-1.0019]	<.0001	1.0012	0.12	[1.0008-1.0016]	0.0031
	Wind Speed	1.0280	2.80	[1.0264-1.0296]	<.0001	1.0360	3.60	[1.0312-1.0409]	<.0001
	Daily Snow	1.0105	1.05	[1.0096-1.0114]	<.0001	1.0124	1.24	[1.0091-1.0158]	<.0001
	$PM_{2.5}$	1.0030	0.30	[1.0028-1.0032]	<.0001	1.0037	0.37	[1.0032-1.0042]	<.0001
Lag 3	Avg. Temp.	1.0143	1.43	[1.0141-1.0145]	<.0001	1.0122	1.22	[1.0118-1.0127]	<.0001
	Daily Rain	1.0016	0.16	[1.0014-1.0017]	<.0001	1.0010	0.10	[1.0006-1.0014]	0.0032
	Wind Speed	1.0280	2.80	[1.0264-1.0296]	<.0001	1.0350	3.50	[1.0301-1.0399]	<.0001
	Daily Snow	1.0079	0.79	[1.0070-1.0089]	<.0001	1.0069	0.69	[1.0034-1.0104]	<.0001
	$PM_{2.5}$	1.0032	0.32	[1.0030-1.0034]	<.0001	1.0032	0.32	[1.0027-1.0038]	<.0001
Lag 4	Avg. Temp.	1.0142	1.42	[1.0140-1.0143]	<.0001	1.0122	1.22	[1.0117-1.0127]	<.0001

	Daily Rain	1.0020	0.20	[1.0019-1.0022]	<.0001	1.0015	0.15	[1.0010-1.0019]	<.0001
	Wind Speed	1.0207	2.07	[1.0190-1.0223]	<.0001	1.0303	3.03	[1.0254-1.0352]	<.0001
	Daily Snow	1.0058	0.58	[1.0048-1.0067]	<.0001	1.0007	0.07	[0.9971-1.0044]	0.4638
	$PM_{2.5}$	1.0027	0.27	[1.0025-1.0029]	<.0001	1.0017	0.17	[1.0012-1.0023]	<.0001
Lag 5	Avg. Temp.	1.0144	1.44	[1.0143-1.0146]	<.0001	1.0123	1.23	[1.0119-1.0128]	<.0001
	Daily Rain	1.0019	0.19	[1.0018-1.0021]	<.0001	1.0012	0.12	[1.0008-1.0016]	0.0029
	Wind Speed	1.0200	2.00	[1.0183-1.0216]	<.0001	1.0248	2.48	[1.0198-1.0297]	<.0001
	Daily Snow	1.0016	0.16	[1.0006-1.0027]	0.0004	1.0013	0.13	[0.9971-1.0055]	0.3975
	$PM_{2.5}$	1.0019	0.19	[1.0017-1.0021]	<.0001	1.0013	0.13	[1.0008-1.0019]	<.0001
Lag 6	Avg. Temp.	1.0145	1.45	[1.0144-1.0147]	<.0001	1.0126	1.26	[1.0121-1.0130]	<.0001
	Daily Rain	1.0016	0.16	[1.0015-1.0017]	<.0001	1.0006	0.06	[1.0002-1.0010]	0.0015
	Wind Speed	1.0189	1.89	[1.0173-1.0205]	<.0001	1.0230	2.30	[1.0181-1.0279]	<.0001
	Daily Snow	1.0011	0.11	[1.0001-1.0022]	0.0010	1.0011	0.11	[0.9970-1.0053]	0.6470
	$PM_{2.5}$	1.0014	0.14	[1.0012-1.0015]	<.0001	1.0011	0.11	[1.0006-1.0017]	0.0041
Lag 7	Avg. Temp.	1.0146	1.46	[1.0144-1.0147]	<.0001	1.0127	1.27	[1.0122-1.0131]	<.0001
	Daily Rain	1.0011	0.11	[1.0010-1.0013]	<.0001	1.0004	0.04	[1.0000-1.0008]	0.0673
	Wind Speed	1.0156	1.56	[1.0139-1.0172]	<.0001	1.0137	1.37	[1.0088-1.0186]	<.0001
	Daily Snow	1.0008	0.08	[0.9998-1.0018]	0.7763	1.0008	0.08	[0.9969-1.0047]	0.5796
	$PM_{2.5}$	1.0005	0.05	[1.0003-1.0006]	0.0015	1.0001	0.01	[0.9995-1.0006]	0.4159

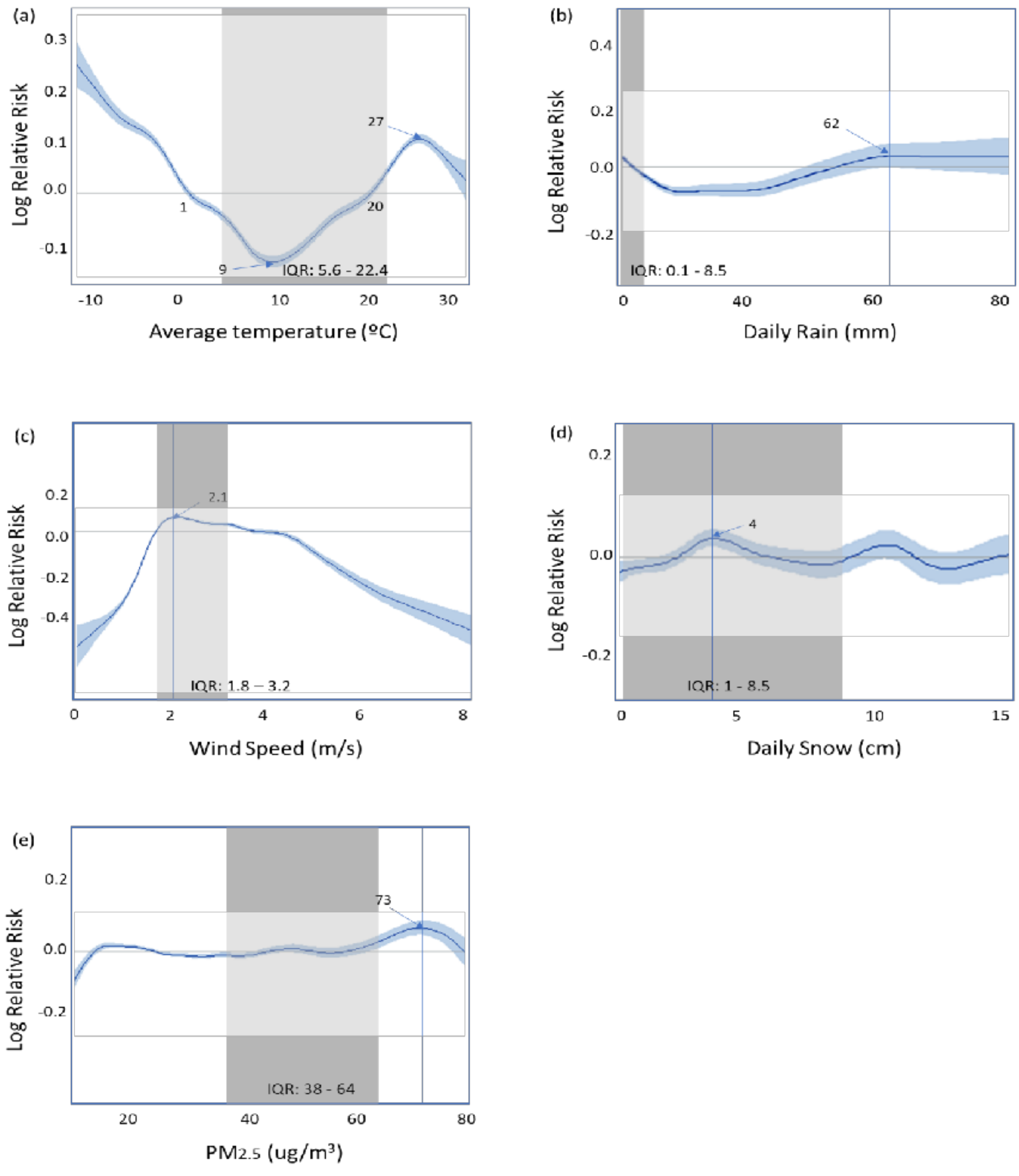
Time	Variables	Spine			
		RR	ER(%)	95% CI	P-value
Lag 0	Avg. Temp.	1.0101	1.01	[1.0099-1.0104]	<.0001
	Daily Rain	1.0010	0.10	[1.0007-1.0012]	<.0001
	Wind Speed	1.0209	2.09	[1.0183-1.0234]	<.0001
	Daily Snow	1.0087	0.87	[1.0069-1.0105]	<.0001
	$PM_{2.5}$	1.0025	0.25	[1.0022-1.0027]	<.0001
Lag 1	Avg. Temp.	1.0101	1.01	[1.0100-1.0102]	<.0001
	Daily Rain	1.0007	0.07	[1.0006-1.0008]	<.0001
	Wind Speed	1.0214	2.14	[1.0203-1.0225]	<.0001
	Daily Snow	1.0085	0.85	[1.0078-1.0093]	<.0001

	$PM_{2.5}$	1.0025	0.25	[1.0024-1.0026]	<.0001
Lag 2	Avg. Temp.	1.0102	1.02	[1.0101-1.0103]	<.0001
	Daily Rain	1.0008	0.08	[1.0007-1.0008]	<.0001
	Wind Speed	1.0234	2.34	[1.0223-1.0245]	<.0001
	Daily Snow	1.0077	0.77	[1.0070-1.0085]	<.0001
	$PM_{2.5}$	1.0021	0.21	[1.0020-1.0023]	<.0001
Lag 3	Avg. Temp.	1.0102	1.02	[1.0101-1.0103]	<.0001
	Daily Rain	1.0008	0.08	[1.0007-1.0009]	<.0001
	Wind Speed	1.0230	2.30	[1.0220-1.0241]	<.0001
	Daily Snow	1.0056	0.56	[1.0048-1.0063]	<.0001
	$PM_{2.5}$	1.0020	0.20	[1.0019-1.0021]	<.0001
Lag 4	Avg. Temp.	1.0102	1.02	[1.0101-1.0103]	<.0001
	Daily Rain	1.0009	0.09	[1.0008-1.0010]	<.0001
	Wind Speed	1.0205	2.05	[1.0194-1.0216]	<.0001
	Daily Snow	1.0046	0.46	[1.0038-1.0054]	<.0001
	$PM_{2.5}$	1.0016	0.16	[1.0015-1.0017]	<.0001
Lag 5	Avg. Temp.	1.0103	1.03	[1.0102-1.0104]	<.0001
	Daily Rain	1.0009	0.09	[1.0008-1.0010]	<.0001
	Wind Speed	1.0176	1.76	[1.0165-1.0187]	<.0001
	Daily Snow	1.0005	0.05	[0.9996-1.0013]	0.6304
	$PM_{2.5}$	1.0015	0.15	[1.0014-1.0016]	<.0001
Lag 6	Avg. Temp.	1.0103	1.03	[1.0101-1.0104]	<.0001
	Daily Rain	1.0008	0.08	[1.0007-1.0009]	<.0001
	Wind Speed	1.0105	1.05	[1.0094-1.0116]	<.0001
	Daily Snow	1.0003	0.03	[0.9995-1.0012]	0.7136
	$PM_{2.5}$	1.0012	0.12	[1.0011-1.0014]	<.0001
Lag 7	Avg. Temp.	1.0103	1.03	[1.0102-1.0105]	<.0001
	Daily Rain	1.0004	0.04	[1.0003-1.0005]	0.0042
	Wind Speed	1.0003	0.03	[0.9992-1.0013]	0.1597
	Daily Snow	1.0001	0.01	[0.9993-1.0009]	0.8279
	$PM_{2.5}$	1.0002	0.02	[1.0001-1.0003]	0.0089

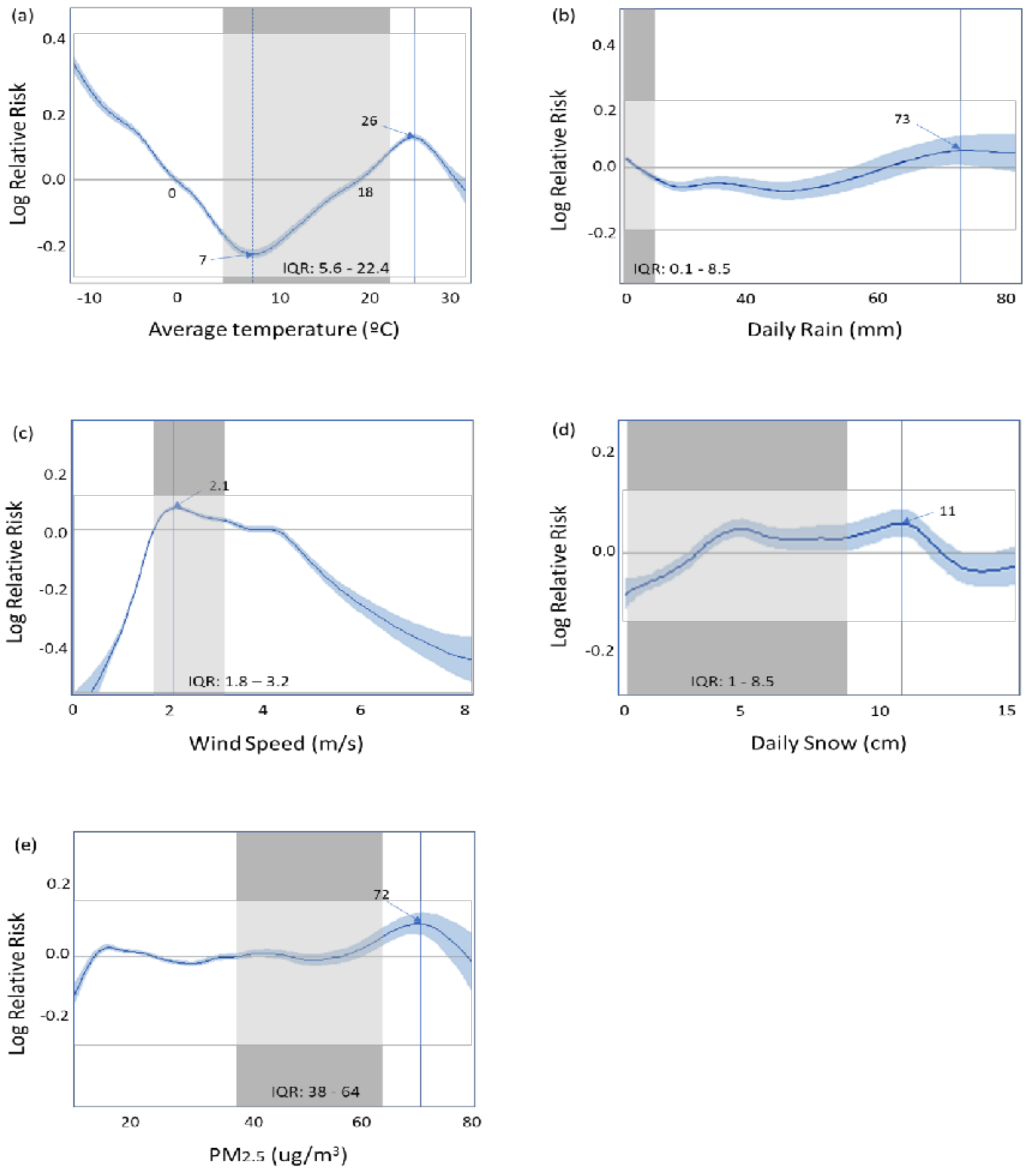
Supplemental Figure 1. Generalized additive model for the effects of selected meteorological factors on the incidence of knee fracture by: (a) average temperature, (b) daily rain, (c) wind speed, (d) daily snow, and (e) particulate matter ≤ 2.5 μm ($PM_{2.5}$). The bold line estimates the relative effect sizes for knee fracture, and the blue area estimates 95% confidence intervals (CIs).The X-axis represents selected meteorological factors. The Y-axes show the relative effect sizes for knee fracture. $PM_{2.5}$, particulate matter ≤ 2.5 μm.



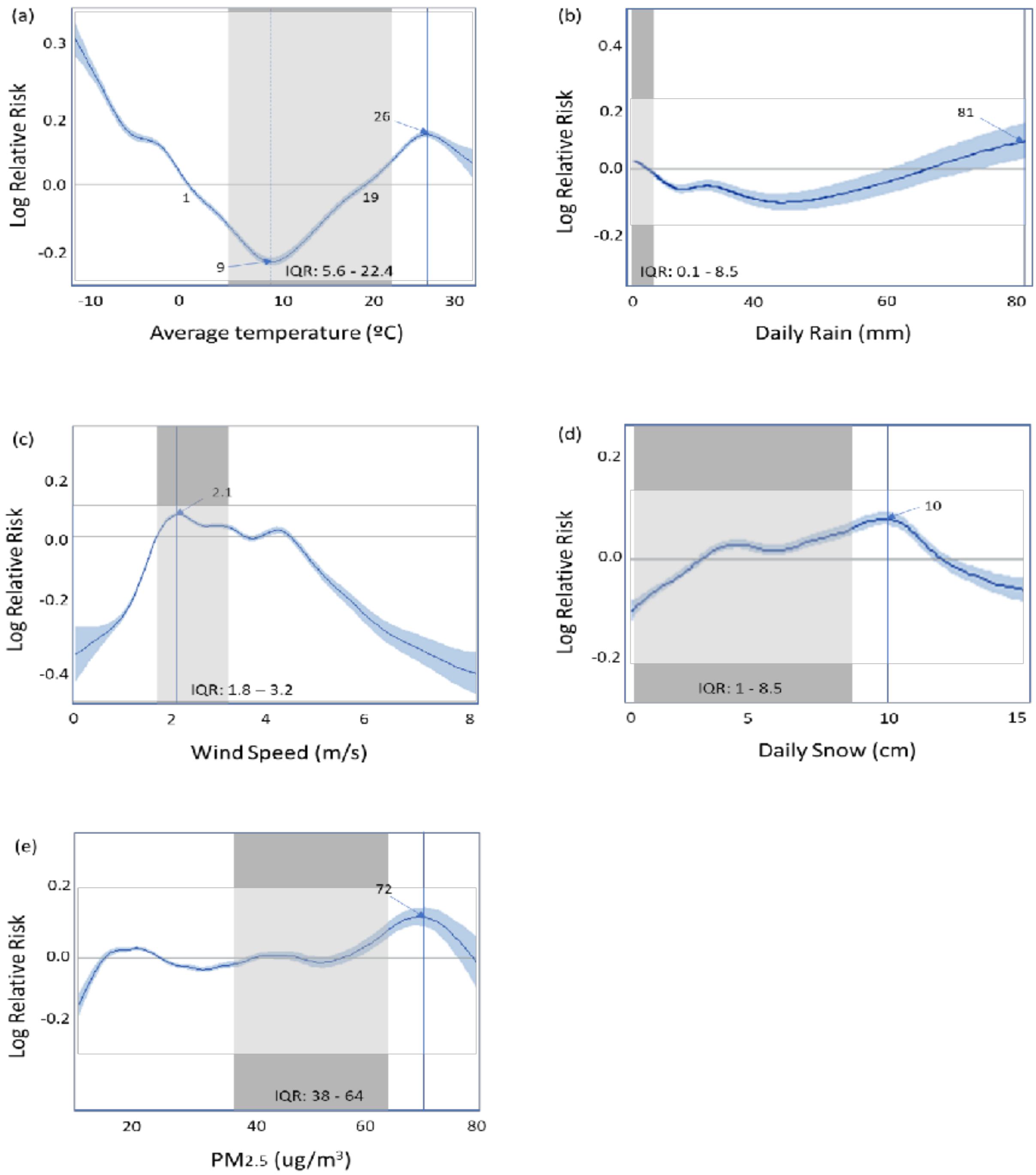
Supplemental Figure 2. Generalized additive model for the effects of selected meteorological factors on the incidence of shoulder fracture by: (a) average temperature, (b) daily rain, (c) wind speed, (d) daily snow, and (e) particulate matter ≤ 2.5 μm ($PM_{2.5}$). The bold line estimates the relative effect sizes for shoulder fracture, and the blue area estimates 95% confidence intervals (CIs). The X-axis represents selected meteorological factors. The Y-axes show the relative effect sizes for shoulder fracture. $PM_{2.5}$, particulate matter ≤ 2.5 μm.



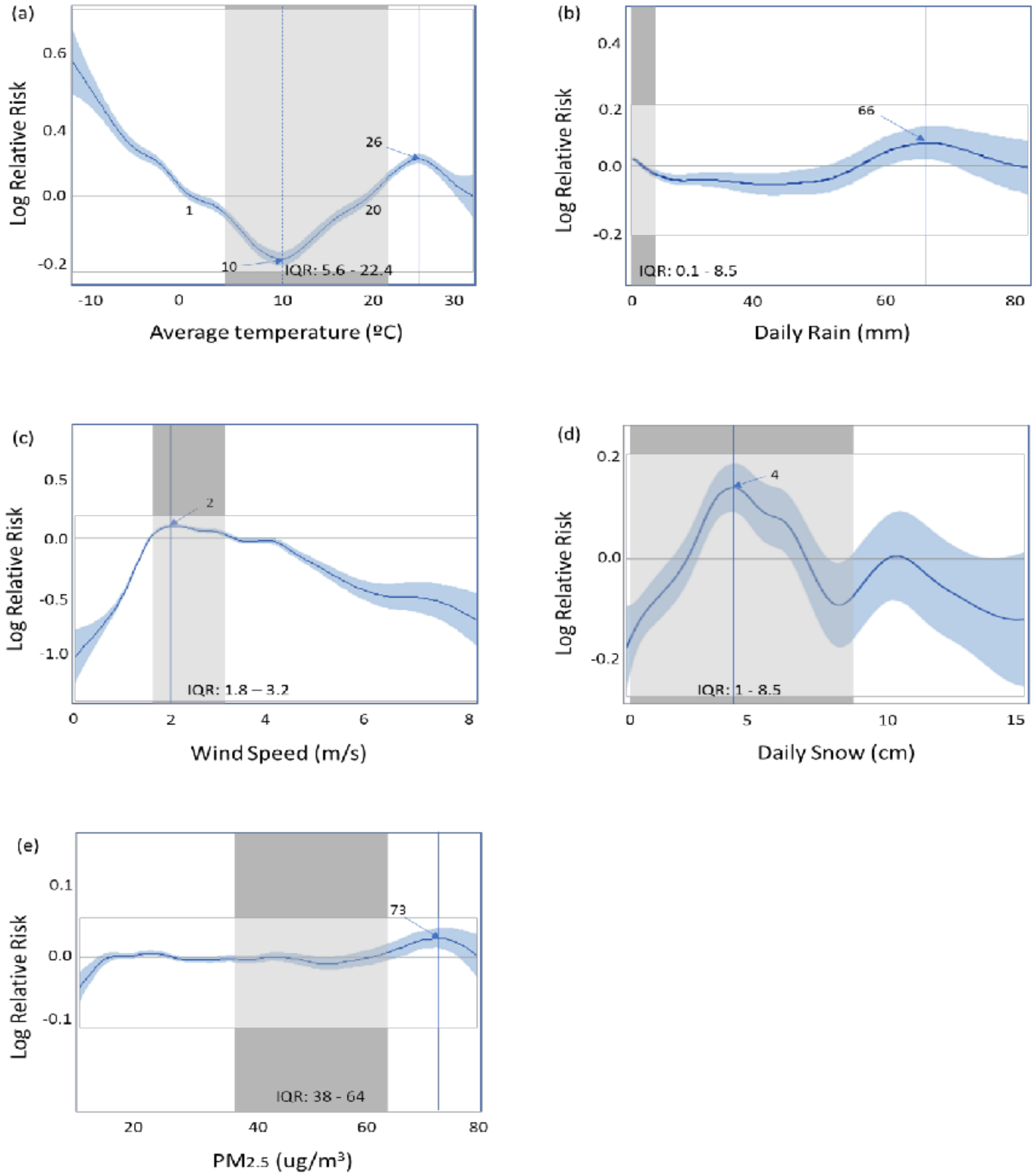
Supplemental Figure 3. Generalized additive model for the effects of selected meteorological factors on the incidence of elbow fracture by: (a) average temperature, (b) daily rain, (c) wind speed, (d) daily snow, and (e) particulate matter ≤ 2.5 μm ($PM_{2.5}$). The bold line estimates the relative effect sizes for elbow fracture, and the blue area estimates 95% confidence intervals (CIs). The X-axis represents selected meteorological factors. The Y-axes show the relative effect sizes for elbow fracture. $PM_{2.5}$, particulate matter ≤ 2.5 μm.



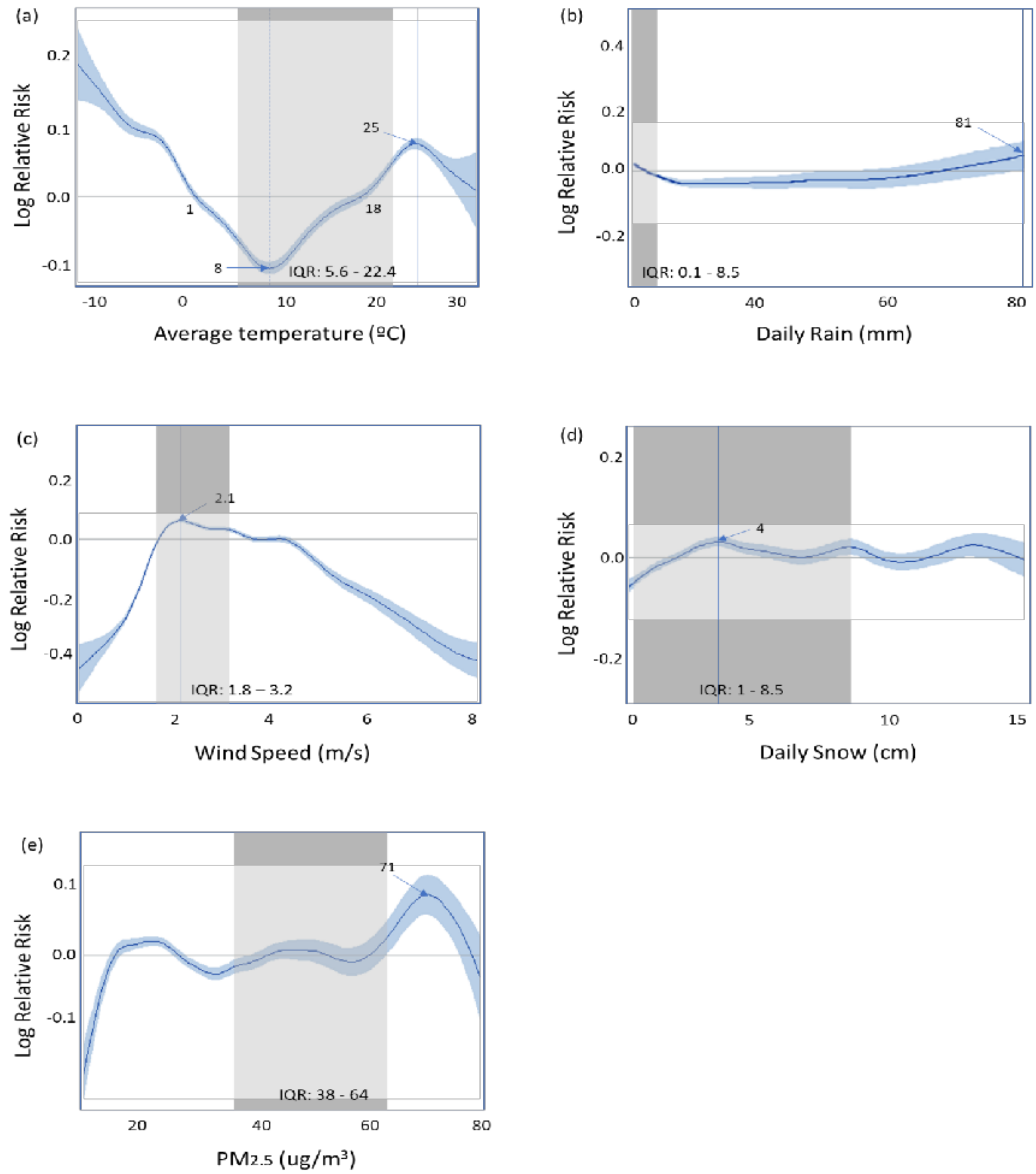
Supplemental Figure 4. Generalized additive model for the effects of selected meteorological factors on the incidence of wrist fracture by: (a) average temperature, (b) daily rain, (c) wind speed, (d) daily snow, and (e) particulate matter ≤ 2.5 μm ($PM_{2.5}$). The bold line estimates the relative effect sizes for wrist fracture, and the blue area estimates 95% confidence intervals (CIs). The X-axis represents selected meteorological factors. The Y-axes show the relative effect sizes for wrist fracture. $PM_{2.5}$, particulate matter ≤ 2.5 μm.



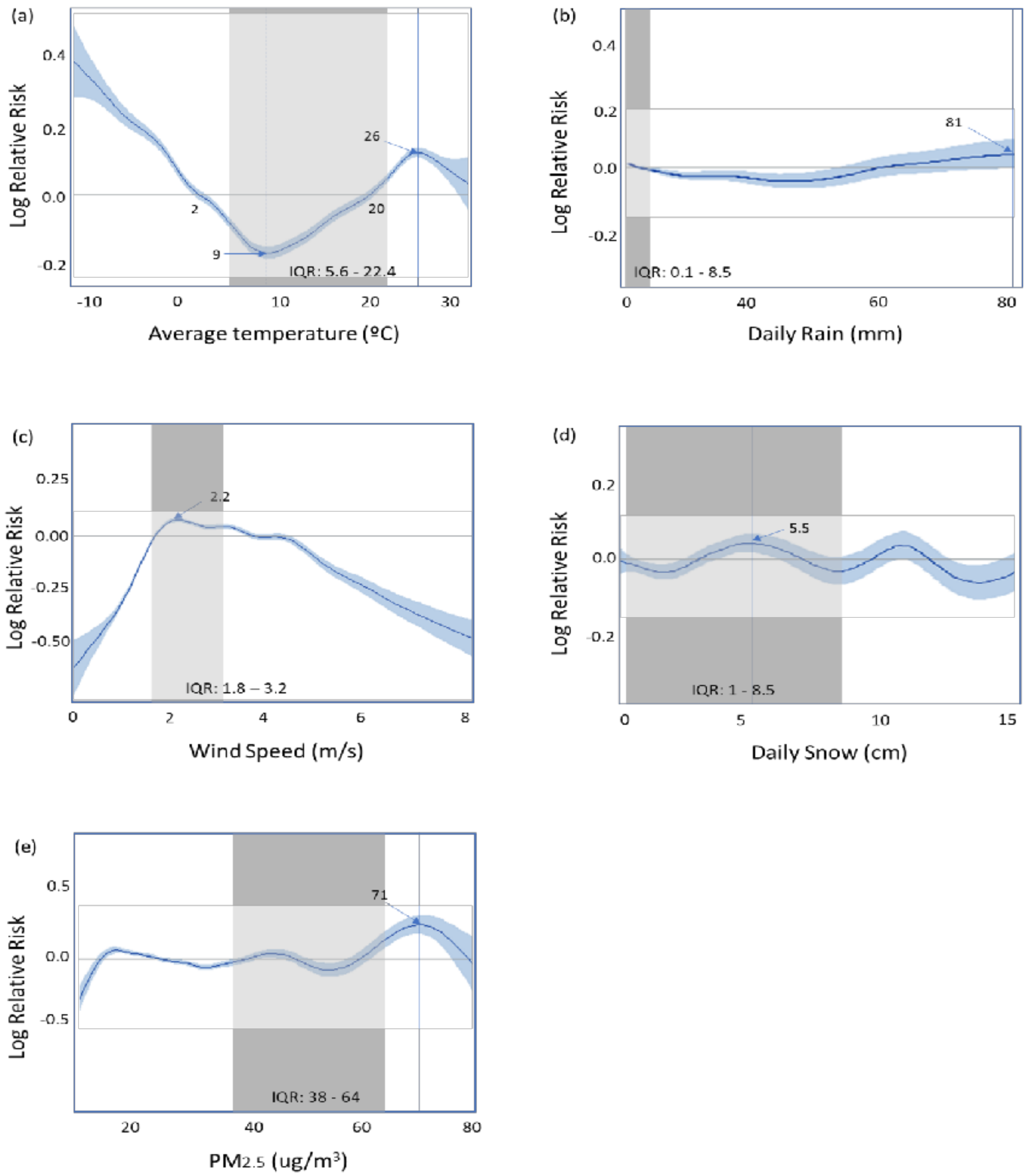
Supplemental Figure 5. Generalized additive model for the effects of selected meteorological factors on the incidence of hand fracture by: (a) average temperature, (b) daily rain, (c) wind speed, (d) daily snow, and (e) particulate matter ≤ 2.5 μm ($PM_{2.5}$). The bold line estimates the relative effect sizes for hand fracture, and the blue area estimates 95% confidence intervals (CIs). The X-axis represents selected meteorological factors. The Y-axes show the relative effect sizes for hand fracture. $PM_{2.5}$, particulate matter ≤ 2.5 μm.



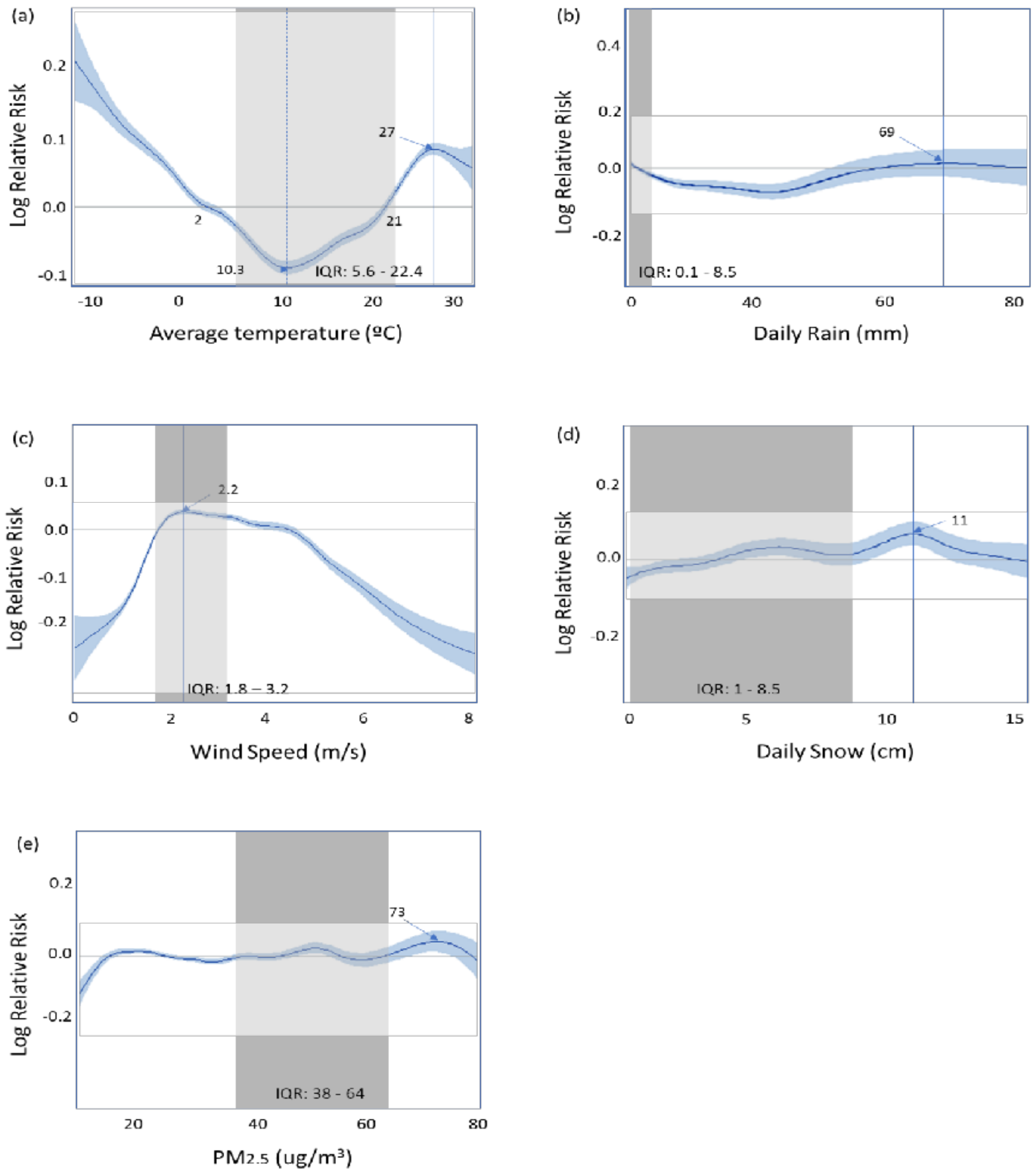
Supplemental Figure 6. Generalized additive model for the effects of selected meteorological factors on the incidence of ankle fracture by: (a) average temperature, (b) daily rain, (c) wind speed, (d) daily snow, and (e) particulate matter ≤ 2.5 μm ($PM_{2.5}$). The bold line estimates the relative effect sizes for ankle fracture, and the blue area estimates 95% confidence intervals (CIs). The X-axis represents selected meteorological factors. The Y-axes show the relative effect sizes for ankle fracture. $PM_{2.5}$, particulate matter ≤ 2.5 μm.



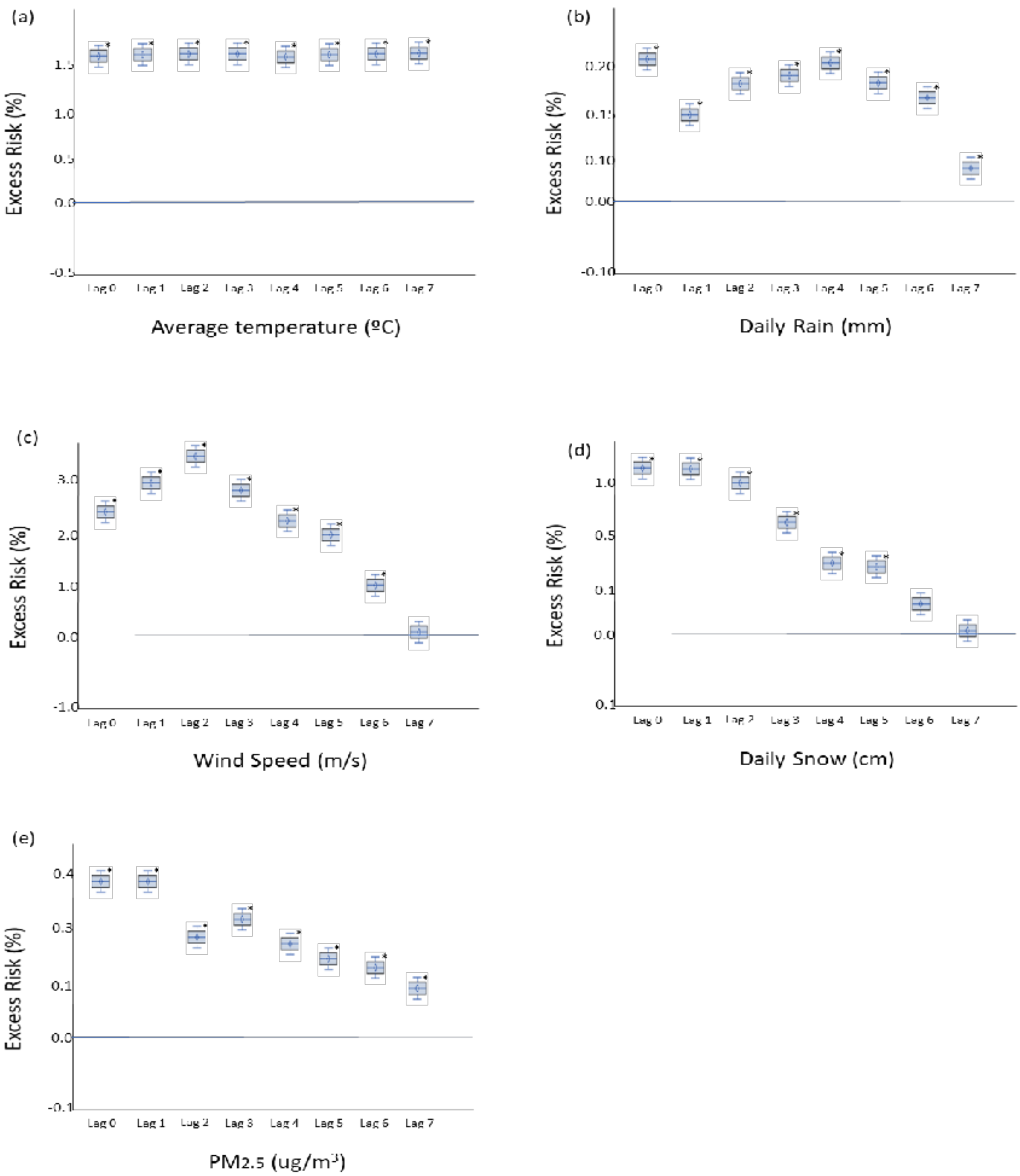
Supplemental Figure 7. Generalized additive model for the effects of selected meteorological factors on the incidence of foot fracture by: (a) average temperature, (b) daily rain, (c) wind speed, (d) daily snow, and (e) particulate matter ≤ 2.5 µm ($PM_{2.5}$). The bold line estimates the relative effect sizes for foot fracture, and the blue area estimates 95% confidence intervals (CIs). The X-axis represents selected meteorological factors. The Y-axes show the relative effect sizes for foot fracture. $PM_{2.5}$, particulate matter ≤ 2.5 µm.



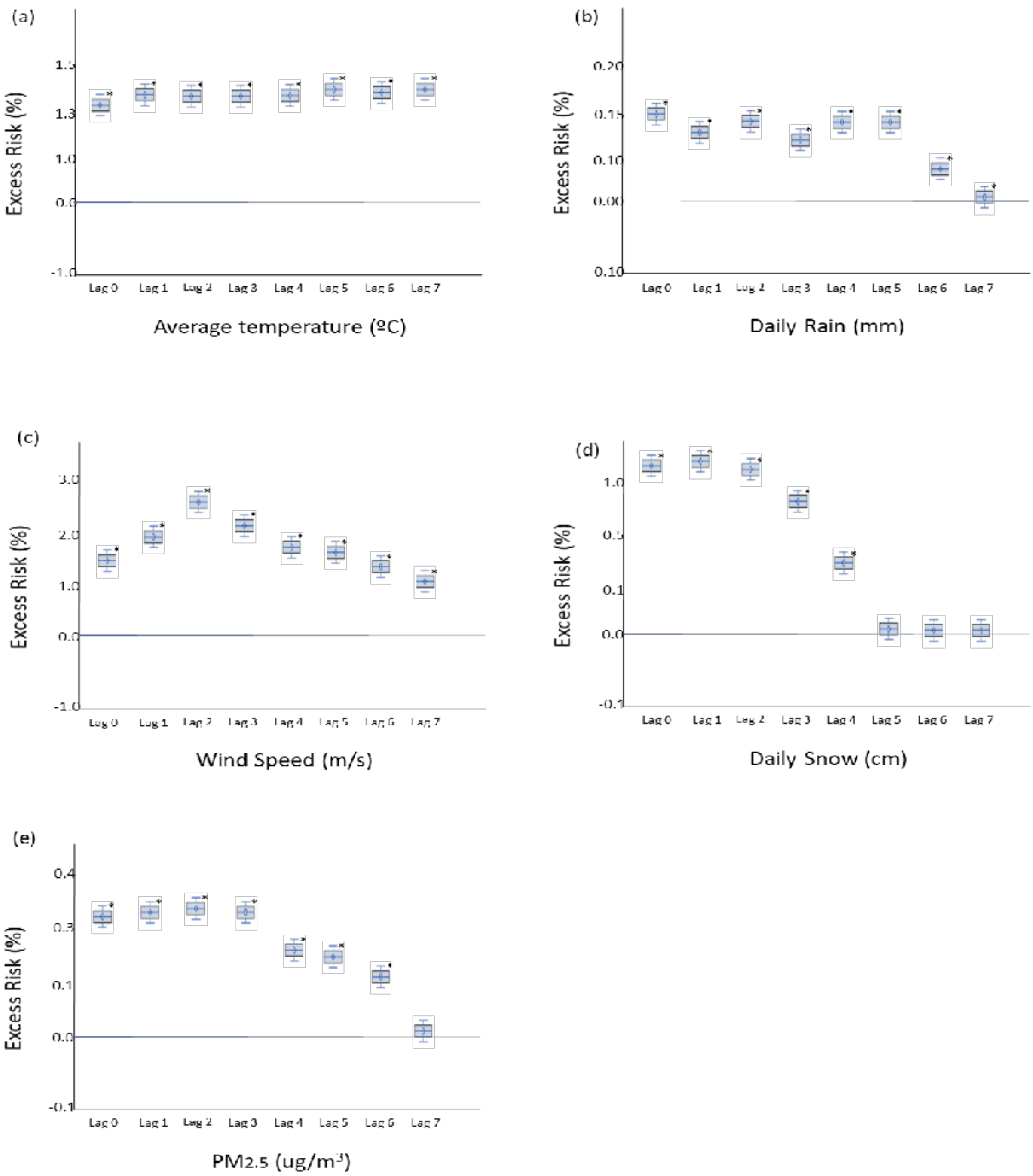
Supplemental Figure 8. Generalized additive model for the effects of selected meteorological factors on the incidence of spine fracture by: (a) average temperature, (b) daily rain, (c) wind speed, (d) daily snow, and (e) particulate matter ≤ 2.5 μm ($PM_{2.5}$). The bold line estimates the relative effect sizes for spine fracture, and the blue area estimates 95% confidence intervals (CIs). The X-axis represents selected meteorological factors. The Y-axes show the relative effect sizes for spine fracture. $PM_{2.5}$, particulate matter ≤ 2.5 μm.



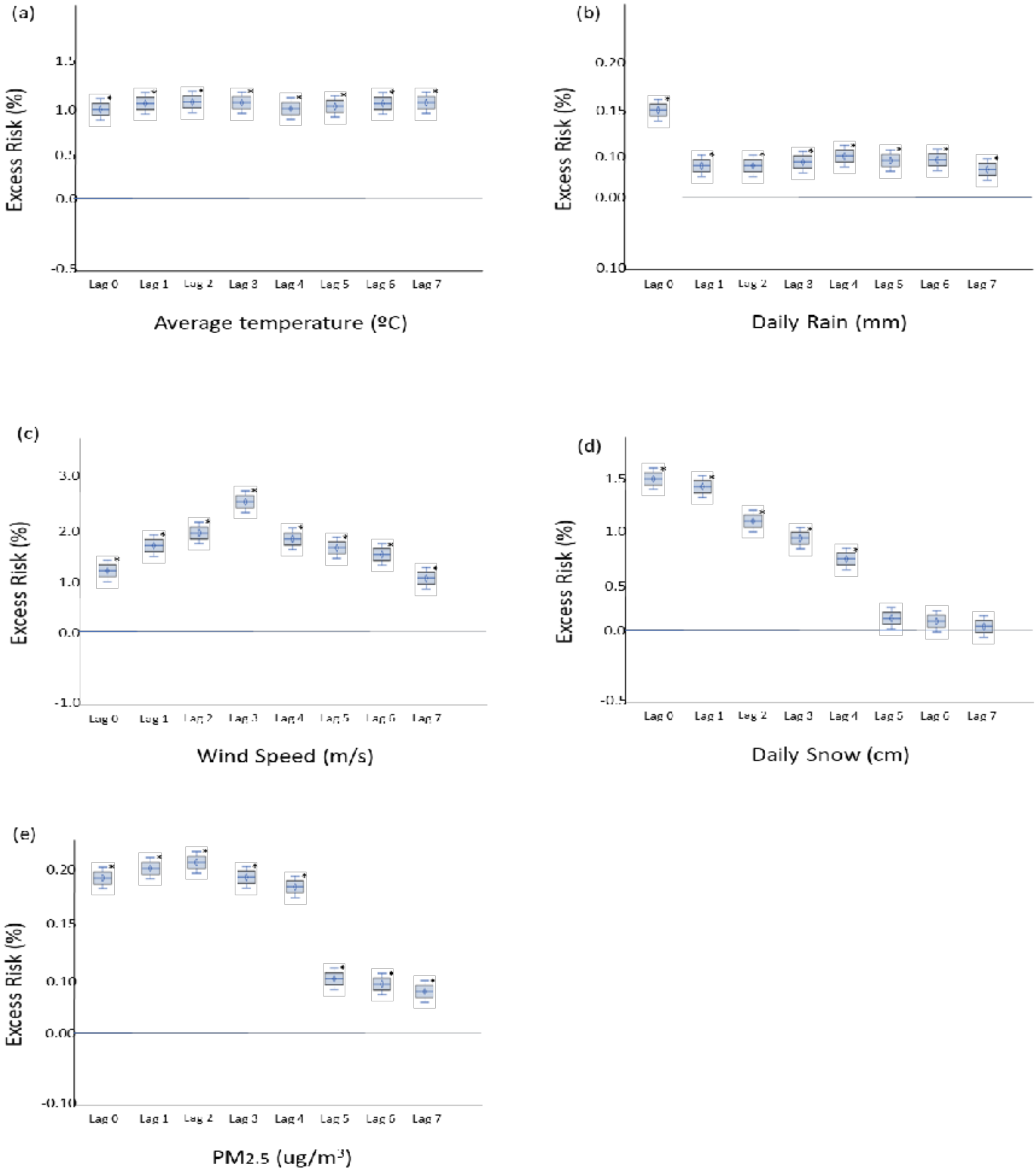
Supplemental Figure 9. Levels of the selected meteorological factors and adjusted excess risks of the knee fracture by: (a) average temperature, (b) daily rain, (c) wind speed, (d) daily snow, and (e) particulate matter ≤ 2.5 μm ($PM_{2.5}$). The Y-axes show the percentages of the adjusted excess risks with 95% confidence intervals (CIs). **P*<.05.



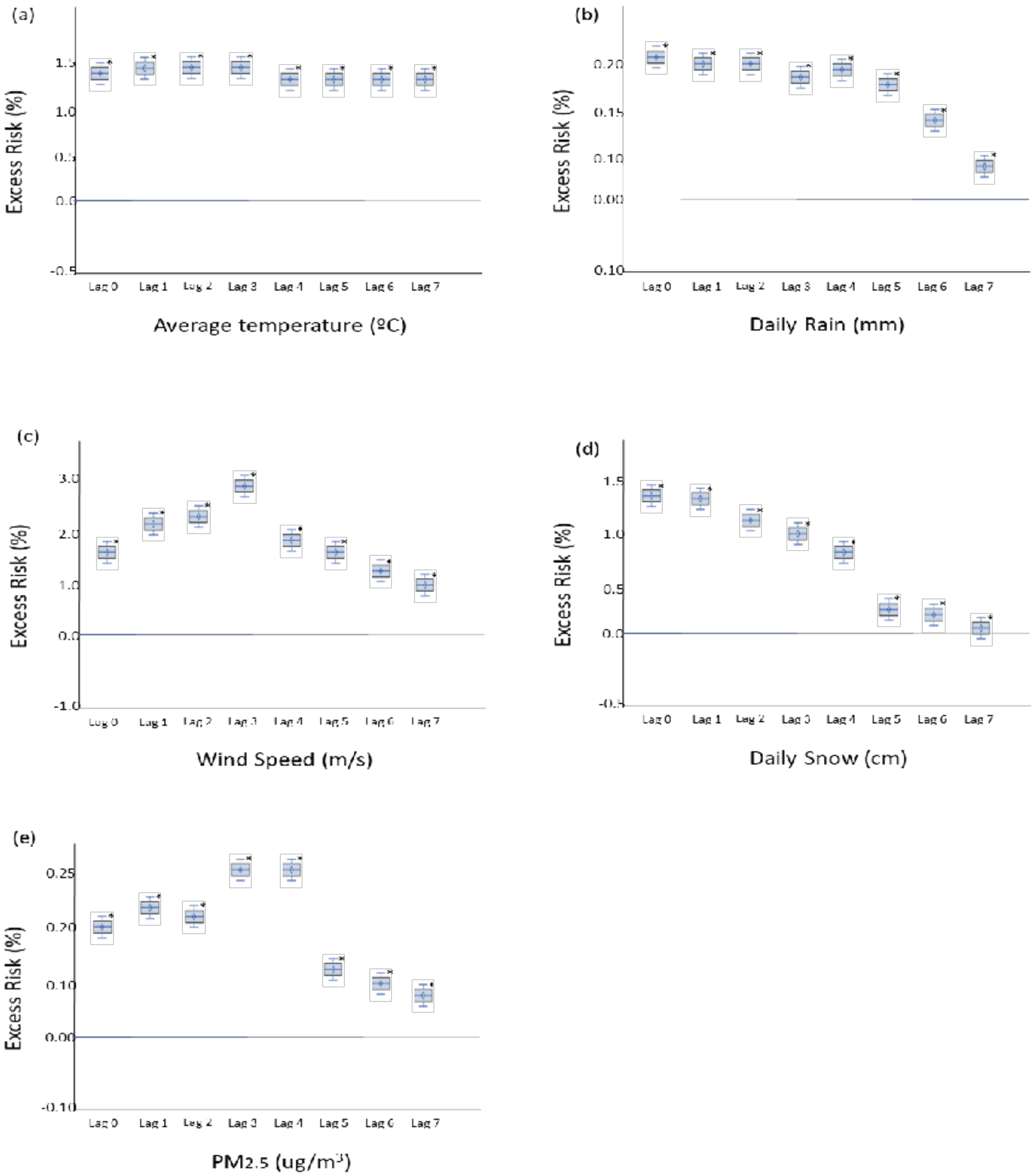
Supplemental Figure 10. Levels of the selected meteorological factors and adjusted excess risks of the shoulder fracture by: (a) average temperature, (b) daily rain, (c) wind speed, (d) daily snow, and (e) particulate matter ≤ 2.5 μm ($PM_{2.5}$). The Y-axes show the percentages of the adjusted excess risks with 95% confidence intervals (CIs). *P<.05.



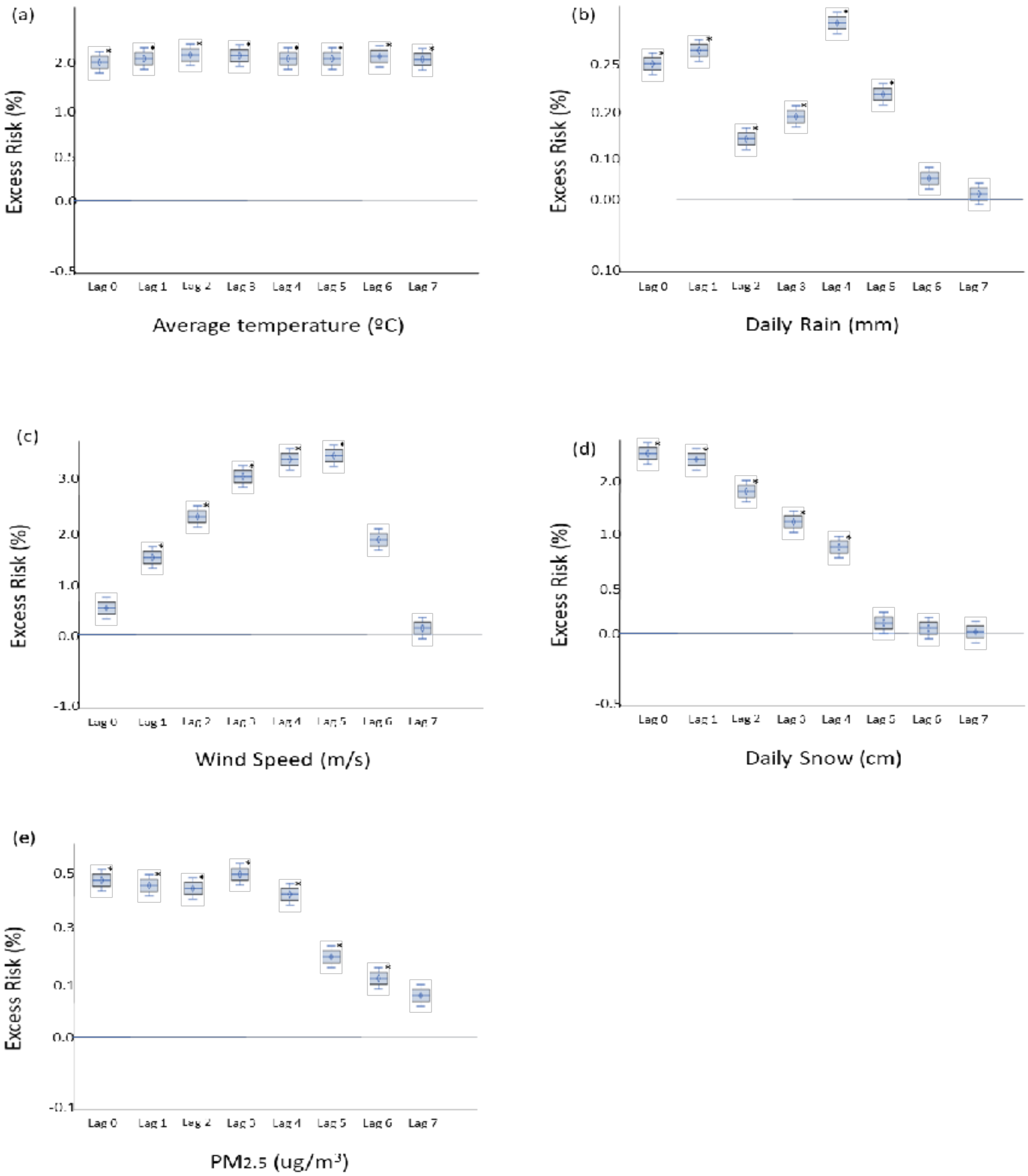
Supplemental Figure 11. Levels of the selected meteorological factors and adjusted excess risks of the elbow fracture by: (a) average temperature, (b) daily rain, (c) wind speed, (d) daily snow, and (e) particulate matter ≤ 2.5 µm ($PM_{2.5}$). The Y-axes show the percentages of the adjusted excess risks with 95% confidence intervals (CIs). *P<.05.



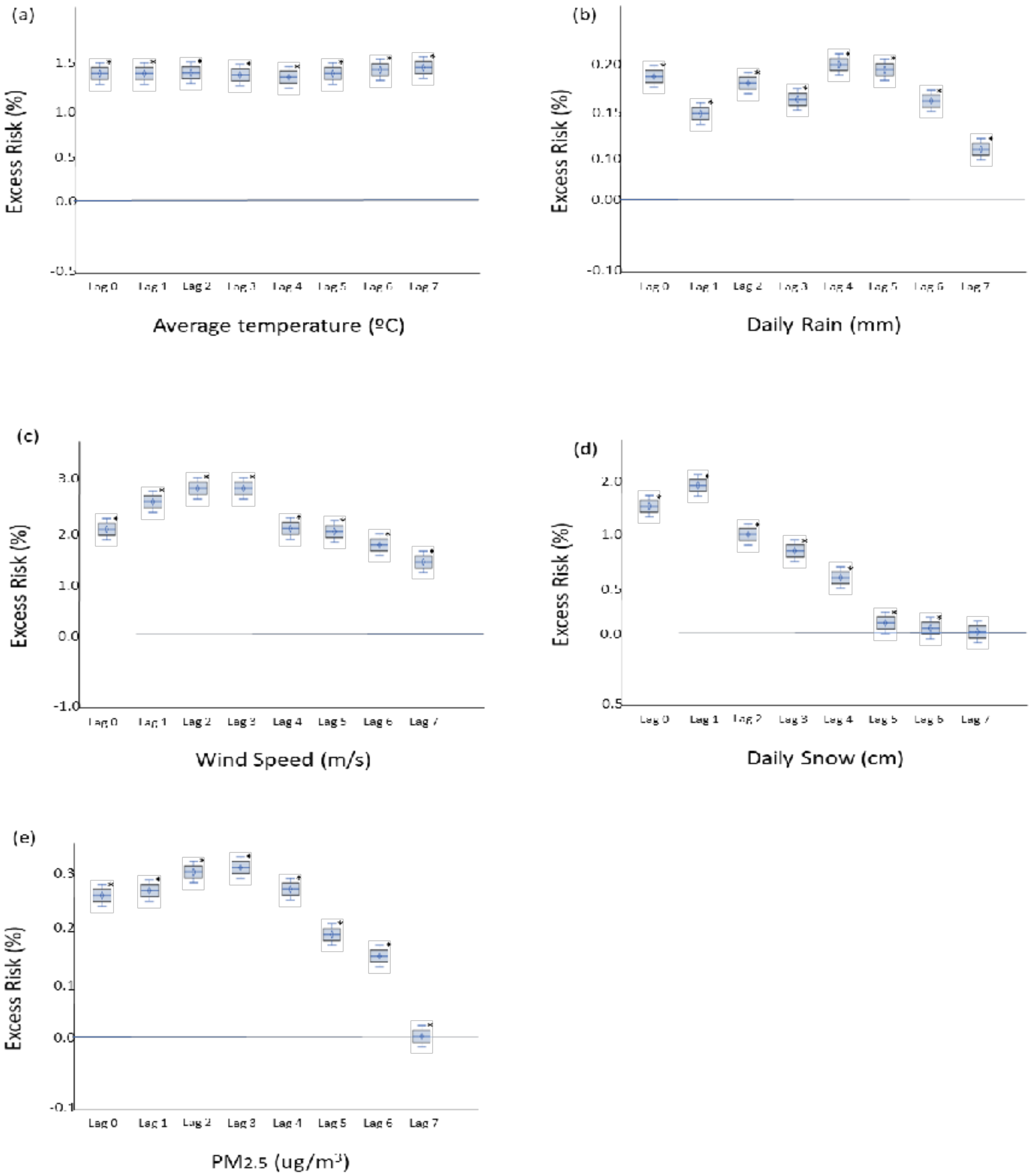
Supplemental Figure 12. Levels of the selected meteorological factors and adjusted excess risks of the wrist fracture by: (a) average temperature, (b) daily rain, (c) wind speed, (d) daily snow, and (e) particulate matter ≤ 2.5 μm ($PM_{2.5}$). The Y-axes show the percentages of the adjusted excess risks with 95% confidence intervals (CIs). *P<.05.



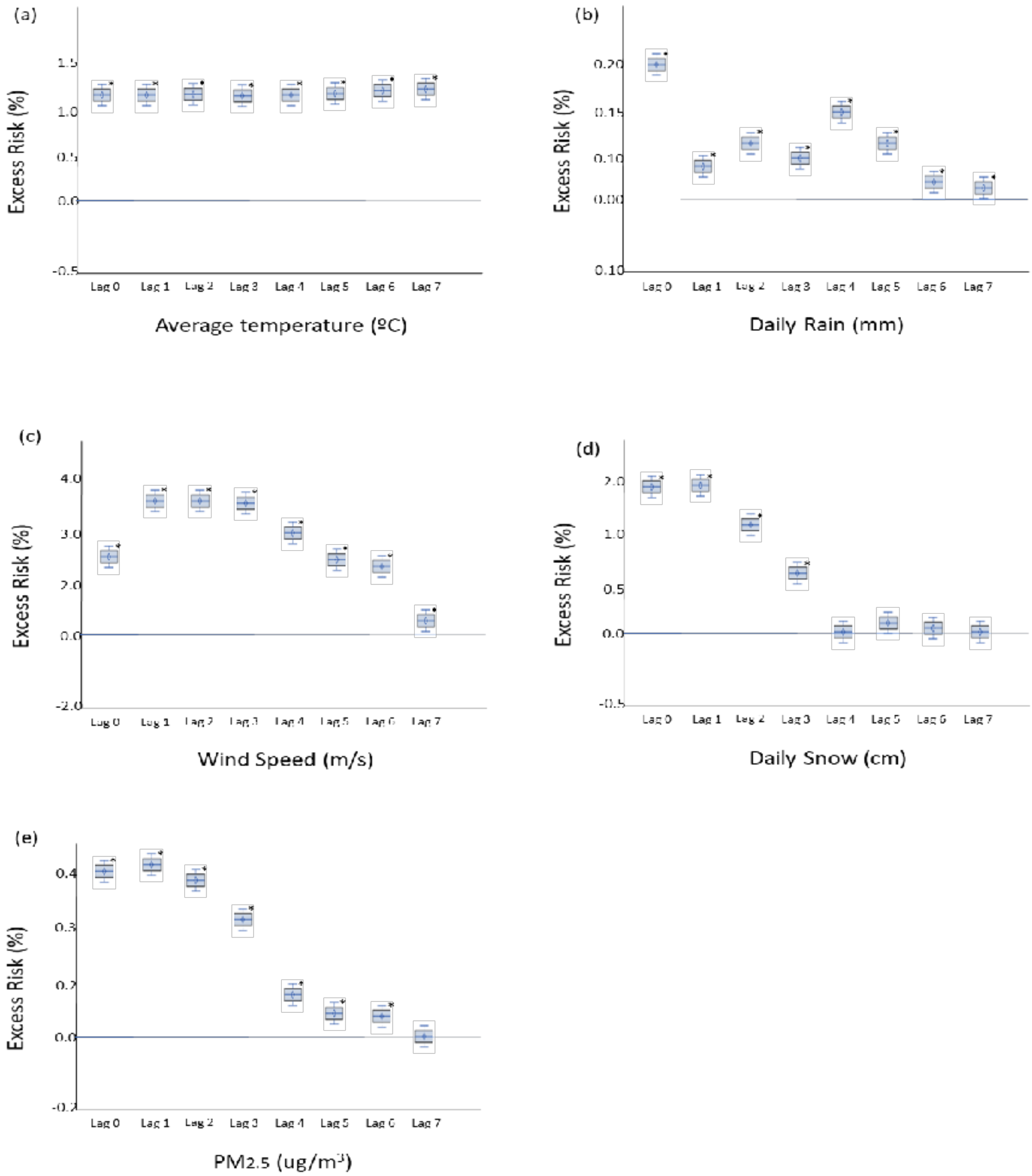
Supplemental Figure 13. Levels of the selected meteorological factors and adjusted excess risks of the hand fracture by: (a) average temperature, (b) daily rain, (c) wind speed, (d) daily snow, and (e) particulate matter ≤ 2.5 μm ($PM_{2.5}$). The Y-axes show the percentages of the adjusted excess risks with 95% confidence intervals (CIs). **P*<.05.



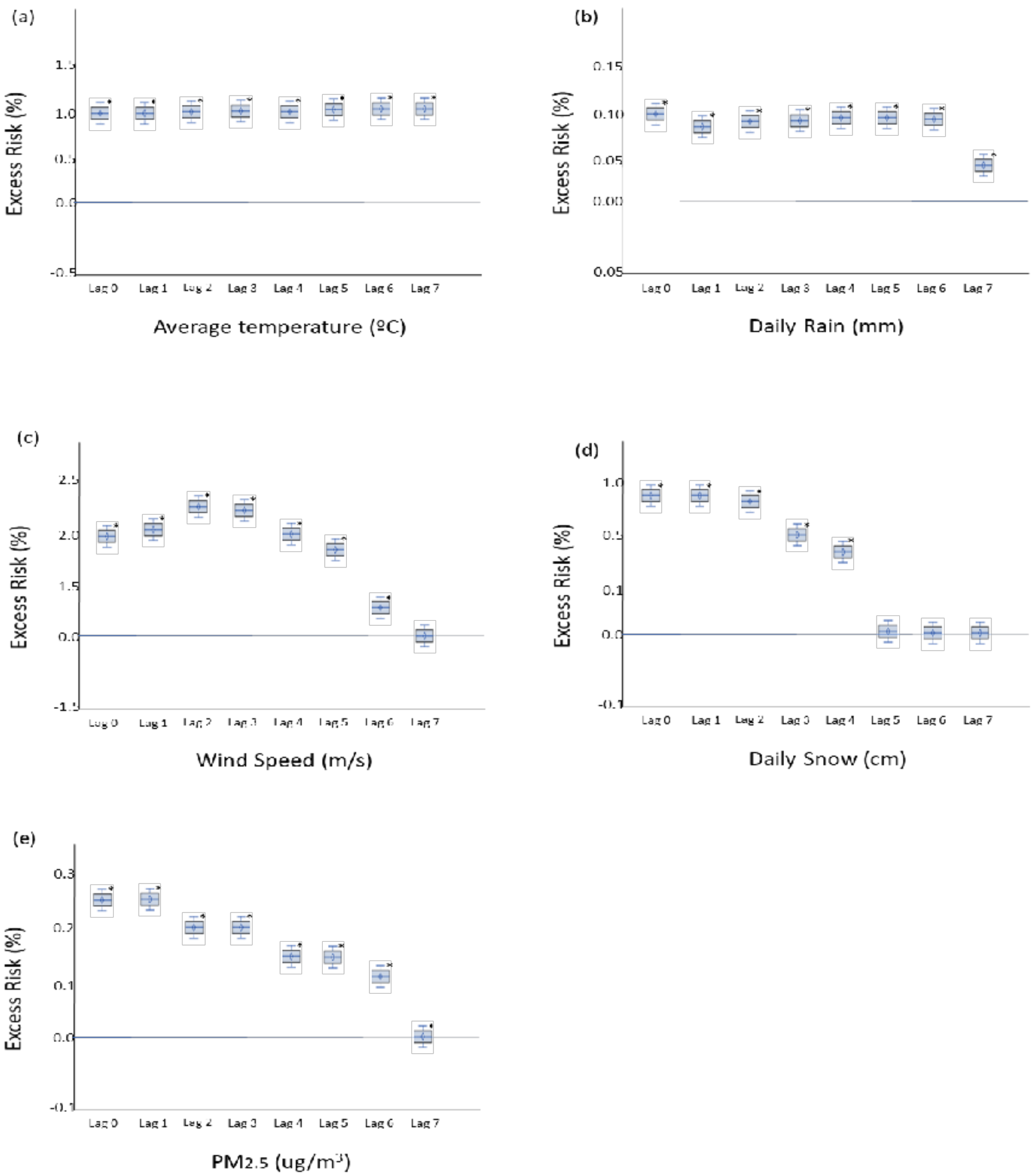
Supplemental Figure 14. Levels of the selected meteorological factors and adjusted excess risks of the ankle fracture by: (a) average temperature, (b) daily rain, (c) wind speed, (d) daily snow, and (e) particulate matter ≤ 2.5 μm ($PM_{2.5}$). The Y-axes show the percentages of the adjusted excess risks with 95% confidence intervals (CIs). *P<.05.



Supplemental Figure 15. Levels of the selected meteorological factors and adjusted excess risks of the foot fracture by: (a) average temperature, (b) daily rain, (c) wind speed, (d) daily snow, and (e) particulate matter ≤ 2.5 µm ($PM_{2.5}$). The Y-axes show the percentages of the adjusted excess risks with 95% confidence intervals (CIs). *P<.05.



Supplemental Figure 16. Levels of the selected meteorological factors and adjusted excess risks of the spine fracture by: (a) average temperature, (b) daily rain, (c) wind speed, (d) daily snow, and (e) particulate matter ≤ 2.5 μm ($PM_{2.5}$). The Y-axes show the percentages of the adjusted excess risks with 95% confidence intervals (CIs). **P*<.05.



STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1,3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (*b*) For matched studies, give matching criteria and number of exposed and unexposed	7 fig1
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7,8
Bias	9	Describe any efforts to address potential sources of bias	17
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding (*b*) Describe any methods used to examine subgroups and interactions (*c*) Explain how missing data were addressed (*d*) If applicable, explain how loss to follow-up was addressed (*e*) Describe any sensitivity analyses	8
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	9 fig1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	9-13
Outcome data	15*	Report numbers of outcome events or summary measures over time	9-13

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	13
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	13-14
Discussion			
Key results	18	Summarise key results with reference to study objectives	14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	17, 18
Generalisability	21	Discuss the generalisability (external validity) of the study results	18
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	20

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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Effect of Meteorological Factors and Air Pollutants on Fractures: A Nationwide Population-based Ecological Study

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Effect of Meteorological Factors and Air Pollutants on Fractures: A Nationwide Population-based Ecological Study

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ABSTRACT

Objective: To determine the association of meteorological factors and air pollutants (MFAPs) with fracture and to estimate the effect size/time lag.

Design: This was a nationwide population-based ecological study from 2008 to 2017.

Setting: Eight large metropolitan areas in Korea.

Participants: Of 8,093,820 patients with fractures reported in the Korea National Health Insurance database, 2,129,955 were analyzed after the dataset containing the patients' data (age, sex, and site of fractures) were merged with MFAPs. Data on meteorological factors, obtained from the National Climate Data Center of the Korea Meteorological Administration. Additionally, data on air pollutants (atmospheric particulate matter of diameter ≤2.5 μm [$PM_{2.5}$], PM_{10}, ozone, nitrogen dioxide, sulfur dioxide, and carbon monoxide) were obtained from the Air Korea database.

Primary and secondary outcome measures: We hypothesized that there would be an association between MFAPs and the incidence of fracture. A generalized additive model was used while factoring in the nonlinear relationship between MFAPs and fractures as well as a time lag ≤7 days. Multivariate analysis was performed. Backward elimination with an Akaike information criterion was used for fitting the multivariate model.

Results: Overall, in eight urban areas, 2,129,955 patients with fractures were finally analyzed. These included 370,344; 187,370; 173,100; 140,358; 246,775; 6,501; 228,346; 57,183; and 719,978 patients with hip, knee, shoulder, elbow, wrist, hand, ankle, foot, and spine fractures, respectively. Various MFAPs (average temperature, daily rain, wind speed, daily snow, and $PM_{2.5}$) showed significant association with fractures; with positive correlations at time lags 7, 5-7, 5-7, 3-7, and 6-7 days, respectively.

Conclusions: Various MFAPs could affect the occurrence of fractures. The average temperature, daily rain, wind speed, daily snow, and $PM_{2.5}$ were most closely associated with fracture; thus, improved public awareness are required on these MFAPs for the clinical prevention and management of fractures.

Article summary

Strengths and limitations of this study

- This study's main strength is that it is the first to investigate the relationship between various MFAPs and fractures.
- Included 2,129,955 sample size, much larger than that of the majority of other studies.
- The limitation included that the study sampled patients who lived in major metropolitan cities, and individual MFAPs exposure levels were not evaluated.
- Individual risk factors could not be covered in the analysis.

Keywords: Meteorological factor, air pollution, particulate matter, weather, fracture.

INTRODUCTION

Fractures are common globally, with reported increasing incidence; they are major public health issues, with a heavy burden on health resources.[1-3] The annual global number of fractures is expected to increase due to aging population.[4] In elderly populations, fractures can not only cause temporary dysfunction but also mortality.[2,5] Advances in surgical techniques and postoperative care have led to lower morbidity and mortality; but recently, attention has turned toward the prevention of fractures. Understanding the circumstances surrounding the occurrence of fractures may provide important information about when and why these injuries occur, and may improve fracture prevention.

The relationship between meteorological factors and air pollutants (MFAPs) and their impacts on fracture incidence have been the subject of many studies; most of which reported that more fractures occur during the winter.[6,7] Several hypotheses have been proposed to explain this association; one hypothesis suggests that MFAPs influence fracture incidence through bone metabolism effects. Reduced exposure to ultraviolet radiation may result in reduced vitamin D synthesis, thereby resulting in vitamin D and parathyroid hormone level changes.[8] It affects bone mineral density (BMD) and muscle strength, which can affect mobility and resistance to falls.[9] However, these effects on bone metabolism are long-term impacts of MFAPs.[10]

Other hypotheses are based on the short-term relationship of MFAPs with the incidence of fracture. Increased risk of falling depends on the weather conditions due to slippery surfaces.[11] Freezing temperatures, rain, snow, and ice may increase the risk of slipping due to the conditions underfoot, and frequent falling is a known risk factor for fractures.[12.13] In low temperatures, there is impaired thermoregulation, hypothermia, and consequent motor coordination deficits that predispose the elderly to falls.[14] Increased risk of falls occurs due to clumsiness in movements. These can explain the many occurrences of fractures, indoors and outdoors.[15] Increased risk of falls can also be due to reduced visual acuity.[16] The presence of haze is associated with increased incidence of fracture. In foggy weather, air pollutants (dust, ash, clay, sand, or ambient air pollutants) are suspended in the atmosphere.[17]

However, most previous studies are focused only on hip fracture or total fractures, without the discrimination of the sites of fractures, specific age groups, and the size and location of hospitals.[10,18,19] There is also insufficient nationwide population-based data. Although previous studies provided information on risk factors of fractures and possible preventive measures for fractures; risk factors, age-specific incidence, and prognoses may differ, depending on the site of fracture. Therefore, it is necessary to determine the association of MFAPs with the occurrence of fractures, by fracture site.[5,20,21]

These hypotheses could help in explaining the results of the association between MFAPs and fracture. Understanding the association between MFAPs and incidence of fracture may lead to improved risk management and the development of appropriate interventions. Thus, this study aimed to determine the association of MFAPs with fracture occurrence, and to estimate their effect size and lag time.

MATERIAL AND METHODS

Data acquisition

It should be mentioned that the study methodology was based on the authors' previous study.[22] The records of patients with fractures were provided by the National Health Insurance Service (NHIS), a government-affiliated agency in Korea. We retrieved the clinical data on bone fractures for both inpatients and outpatients between 2008 and 2017. The sites of bone fractures are as defined in the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) codes with surgical codes: hip (S72.0-S72.3 and S72.7-S72.9); knee (S72.4 and S82.0-S82.2); shoulder (S42.0-S42.3); elbow (S42.4, S52.0-S52.4, and S52.7-S52.9); wrist (S52.5-S52.6); hand (S62 and T10); ankle (S82.3, and S82.5-S82.6); foot (S92, and T12); and spine (S32.0-S32.2, S32.7-S32.8, S22.0-S22.1, and T08). During the study period (2008-2017), we collected 8,093,820 diagnoses of patients with bone fractures and extracted data from the major metropolitan areas, including Seoul, Inchon, Daejeon, Gwangju, Daegu, Ulsan, Busan, and Jeju in Korea. The number of all the patients with fractures in 8 urban areas was 2,129,955 after the dataset containing the patients' data were merged with MFAPs. Data on the general meteorological factors were obtained from the Korea Meteorological Administration National Climate Data Center while those of air pollutants, such as particulate matter, carbon monoxide, and ozone were from Air Korea, during the same period.

Ethical consideration

The study was reviewed and exempted from the requirement of written informed consent by the Institutional Review Board of Gachon University Gil Medical Center (approval number:GCIRB2019-039), which was waived due to the retrospective nature of this study. The study methods were carried out based on the Declaration of Helsinki.

Patient and public involvement

The patients and the public were not involved in the study.

Statistical analysis

Statistical analyses were conducted in SAS version 9.4 for Windows (SAS Institute, Cary, NC). The results are presented as the relative risk ratio (RR) with 95% confidence intervals (CIs). A *P*-value of less than 0.05 was considered significant.

Models

We performed a time-series analysis that mainly used a generalized additive Poisson regression model (GAM) to control for trends, seasonality, covariates, and the day of the week. Meteorological and air pollutant data were used to calculate the daily average, excluding the outliers in pollution variables on the days when the levels of particulate matter ≤ 2.5 μm in diameter ($PM_{2.5}$) was > 120 μm/m^3. In the time-series analysis, GAM leads to unstable estimates due to autocorrelation between meteorological factors and the sites of bone fractures. Thus, we considered that the time lags until the autocorrelation are 'white noise,' shown 7 days after the sites of the bone fracture occurrences. The sum of autocorrelation terms was included as a covariate in GAM. Moreover, we compared the Akaike Information Criterion (AIC) value among meteorological factors and air pollutants for each candidate model using backward elimination for a better fit of the model. Each fracture site had the lowest AIC value when the model included average temperature (AT), daily rain (DR), wind speed (WS), daily snow (DS), and $PM_{2.5}$.

Our final multivariable model is given as follows;

$$\text{Log}[\text{E(Y)}] = \alpha_0 + S\,(\text{AT}, df = 9) + S\,(\text{DR}, df = 9) + S\,(\text{WS}, df = 9) + S\,(\text{DS}, df = 9) + S\,(\text{PM}_{2.5}, df = 9) + offset\,(\log\,(\text{province population})) + \gamma\,(\text{day of week}) + \gamma\,(\text{year}) + \sum_{1 \le \theta \le 7} AR_7$$

where Log[E(Y)] is the logged expected number of the daily fracture occurrences, α_0 is the intercept, *S* are the smooth functions of the meteorological factors using natural cubic splines, *offset* is for the provincial population; γ is the indicator variable for the day of the week and year, while overall autocorrelation effect can be expressed as $AR_1 + \ldots + AR_7$ for 7 lag days.

RESULTS

From a total of 8,093,820 cases of fractures identified during the 10-year study period in 8 urban areas, there were 2,129,955 patients with fractures overall. These included 370,344; 187,370; 173,100; 140,358; 246,775; 6,501; 228,346; 57,183; and 719,978 patients with hip, knee, shoulder, elbow, wrist, hand, ankle, foot, and spine fractures, respectively (Figure 1). Of all the fractures, the spine (33.8%) and hip (17.4%) fractures had the largest proportions. The incidence of fractures increased continuously over the study period. Summaries of the number of fractures by age and sex, are presented in Figure 2. And the mean and SDs of MFAPs data, by years of exposure to MFAPs, are presented in Supplemental Table 1. Among the 13 MFAPs, AT, DR, WS, DS, and $PM_{2.5}$ had the lowest AIC and were selected for further analyses (Supplemental Table 2). Models including these five selected MFAPs showed statistically significant association with the incidence of fracture.

The predictive models for hip fracture incidence using the univariate GAM are shown in Figure 3. AT showed a typical significantly inverted U-shape correlation ($P < .001$), and fracture was higher in both extremes of AT. A negative risk was seen, from -2°C to 21°C, with the highest risk at -7°C. Furthermore, there was an abrupt increase in the risk of hip fracture at extreme temperatures (<-2°C and >21°C). The risk associated with rising DR constantly increased, with a linear correlation, with the incidence of hip fractures ($P<.001$). DR had a negative and positive relative risks at <60 mm and >60 mm, respectively. There was a significant association between hip fracture and WS ($P<.001$), with the highest risk at 1.9 m/s^2. There was a significant association between hip fracture and DS ($P<.001$), with a gradual S-shape curve. Moreover, there was a significant association between hip fracture and $PM_{2.5}$ levels ($P<.001$). An excess risk was seen in the most frequently observed interval (interquartile range [IQR]: 38–64 $\mu g/m^3$).

Fractures at all other sites showed consistent patterns in relation to MFAPs (Supplemental Figures 1-8).

For the five selected variables, time lags were analyzed using multivariate GAM to identify in which prolonged exposure time lag for each variable affects the incidence of fracture (Supplemental Table 3). All the five selected MFAPs showed a maximum lag period of 7 days in the impulse response functions analysis, with no further effect beyond this time point. The box-plot models of the estimated risk for fracture for the five MFAPs are shown in Figure 4.

The multivariate analyses provided the time lags for the effects of the MFAPs on the risk of hip fracture. An increase in AT reflected a significant increase in the risk of hip fracture until 7 days later. The effect of DR, WS, DS, and $PM_{2.5}$ were inversely correlated with the lag time with significantly positive associations, 5–7 days before the occurrence of hip fracture.

The results for the time lags also showed consistent patterns in fractures at all other sites (Supplemental Figures 9-16).

DISCUSSION

In our analysis of the nationwide data of the association between fracture and MFAPs, we found

AT, DR, WS, DS, and $PM_{2.5}$ to be closely associated with fracture, among various MFAPs. These selected MFAPs were shown to affect fractures, up to 7 days later. Our evaluation was based on the short-term relationship between the daily variations in different MFAPs and the daily incidence of fractures, which occurred due to the increased risk of falling from adverse MFAPs. This would explain the significantly positive correlations between fractures and several MFAPs. Our study strengthens the importance of the association of various MFAPs in the incidence of fractures. Fractures at all other sites showed a consistent pattern in relation to MFAPs.

Globally, fractures are important public health problems because of the related morbidity and mortality, diminished health-related quality of life, and associated costs. Despite the development of effective surgical treatments, the cost of surgery and subsequent disabilities, make the prevention of fractures an integral part of any strategy to reduce the impact of fractures, especially considering the aging trend of the population.[23]

Most fractures are not due to a single cause, but from multiple interactions between individuals and the environment.[24] The reason for the increased number of fractures in adverse MFAPs is not well understood. Recent studies have shown that seasonal patterns observed in fractures may be related to weather patterns such as temperature, snow, or ice.[13,25] However, these previous studies reported associations between fractures and weather data driven by the seasonal factors, not by the daily variability in incidence of fractures. Moreover, analyses of the relationship between fractures and MFAPs using day as the unit of analysis are very rare in the literature.

Several mechanisms have been proposed for the short-term relationship between incidence of fractures and various MFAPs. The mechanisms of fractures in each site appeared to be similar, because fractures at all other sites showed a consistent pattern in relation to MFAPs.

AT, DR, WS, and DS were shown in our study to correlate with a rise in incidence of fractures. Past research has shown that slippery conditions greatly enhance the incidence of fractures, explaining this relationship.[26] DR had a negative relative risk at >60 mm and a relatively positive risk at <60 mm. This can be explained by the fact that when it rains, although people do not go outside; however, with more rain, the road becomes more slippery and traffic accidents increase. DS showed a gradual S-shape curve, or an irregular pattern, due to the few days of snow. Jacobsen et al. associated MFAPs (snow and ice) with the incidence of hip fractures, and observed a significant increase in its incidents, consistent with that with frozen rain.[6] Levy et al. reported a significant increase in the incidence of hip fractures on days with freezing precipitation.[25] Lau et al. concluded that AT is a more important independent risk factor of hip fracture.[27]

We found that AT was closely related to a higher incidence of fractures. A possible mechanism is that weather conditions affect activity levels.[28] Lower temperatures is a cause of blood pressure and hemodynamic changes, and dexterity decreases, leading to increased falls and fractures.[29] It can also reduce physical activity, leading to impaired coordination and consequently, bone fragility.[30] The more cold people feel, the more likely they are to wear extra clothes, which may make them clumsier. Darker and colder weather may increase the number of falls.[15] Even though many falls occur indoors, changes in activity levels due to prevailing weather conditions lead to changes in the risk of falls and fracture rates. These provides plausible explanations for why fracture rates are higher on cold days.[28]

Several studies have included the wind as an MFAP variable, in their analyses. One possible explanation could be that the greater the exposure to the wind, the greater the risk of falling. Lau et al. found an excessive incidence of hip fractures in more windy days.[27] Mirchandani et al.

found a significant correlation between WS and the incidence of hip fractures.[30] Jacobsen et al. observed an increase in the risk of hip fractures with high WS days.[6] Tenias et al. also confirmed increased hip fracture risk in more windy days.[23]

The mechanisms of the relationship between air pollution and incidence of fracture is still unclear. Several studies have investigated the possible relationship between air pollution, BMD, and fractures.[31-33] Alvaer et al. found associations between osteoporosis, forearm fractures, and air pollution. An inverse association was found between BMD and air pollution.[32] Prada et al. found an association between long-term exposure to $PM_{2.5}$ and osteoporosis-related fractures.[34] Chang et al. showed a tendency of increase in association between air pollution and risk of osteoporosis, suggesting that exposure to air pollution could increase the risk of osteoporosis.[31] Therefore, if reduced bone resistance is the mechanism by which air pollution is involved in hip fracture, there would be no effect in the short-term.

What we are actually observing is that air pollution increases the risk of falls.[17] Reduced visual acuity has long been regarded as a risk factor for fracture.[18,35] The reduced hours of sunlight and increased air pollution reduce visual acuity, which predisposes to falls and hip fracture.[16] In a large-scale cohort study, reduced visual acuity increased the likelihood of falls and fractures in the elderly population.[18] Also, acute exposure to $PM_{2.5}$ can stimulate the autonomic nervous system (ANS), increasing the risk of arrhythmia, orthostasis, and syncope.[36] Therefore, $PM_{2.5}$ exposure has been associated with changes in heart rate in the elderly.[37] Reduced heart rate variability due to impairment of ANS could increase the risk of falls.

Our observations on the association of MFAPs with fractures can help in developing the prevention strategies for fractures. The elevated incidence during winter implies that we should raise awareness on the risk of slippery conditions, the importance of keeping warm, improved lighting conditions, and avoiding the wearing of cumbersome clothing.[38]

There were also some limitations in our study. First, we sampled patients who lived in major metropolitan cities. Weather stations are sparsely placed in rural areas, thus we ruled to exclude rural areas owing to the concern of unreliable data. Second, individual MFAPs exposure levels were not evaluated, and we assumed that individuals were exposed to identical environments. Therefore, the possibility of ecological fallacy should be noted. Third, individual risk factors such as comorbidities and lifestyle, which would affect fracture occurrence could not be controlled in the analysis. Fourth, the decision of whether fracture occurred was only dependent on the diagnostic codes, thus the validity of healthcare claims data diagnosis on fracture is debatable. We included only inpatient records to reduce the possibility of coding inaccuracies in our dataset. Painless, undiagnosed, and self-resolved fractures were not included, and there may be a difference between the actual incidence of fracture and the onset of symptoms. Fifth, if citizens tend to stay indoors depending on the level of fine dust, potential bias can occur when special weather forecasts are announced such as by the fine dust warning service. Moreover, discordance between the actual residential areas and weather stations could be found. Finally, the mechanisms underlying the effect of each MFAPs on fracture occurrence could not be identified.

However, our study has several strengths. First, this study was the first to investigate the relationship between various MFAPs and fractures. Second, because we used national-level NHIS data, we had the advantage that our study included a sample size of 2,129,955, much larger than that in the majority of other studies. As a result of the single-payer universal healthcare coverage in Korea, the catchment of fractures was expected to be very high. These facilitated the analyses of a large and credible dataset, which is often hard to implement in other countries. Third, we investigated the relationship between all 13 MFAPs portrayed by the Korean Meteorological Administration, and this allowed a plausible review of the real-world influences and interactions of $PM_{2.5}$ with diverse MFAPs. Fourth, the current study was representative of the capital city and seven other areas in Korea, which could reduce bias by diminishing the region-specific effects such as race, ethnicity, economic levels, and accessibility to the hospitals. Fifth, time series Poisson analysis was used with GAM to consider the interaction among MFAPs in terms of fracture occurrence.

CONCLUSIONS

In conclusion, we investigated the relationship between MFAPs and fracture based on healthcare claims and data from a meteorological database. AT, DR, WS, DS, and $PM_{2.5}$ were identified as MFAPs that were most closely associated with fracture. These MFAPs maintained influence for a maximum of 7 days. Visualization of the effect-time association of MFAPs with fracture was possible in the model. In the future, further confirmatory studies and improved public awareness regarding the MFAPs that are related to the incidence of fracture are needed for the clinical prevention and management of fractures.

Acknowledgements

Ethics approval and consent to participate: The study was reviewed and exempted from the requirement of written informed consent by the Institutional Review Board of Gachon University Gil Medical Center (approval number:GCIRB2019-039), which was waived due to the

retrospective nature of this study. The study methods were carried out based on the Declaration of Helsinki.

Availability of data and materials: The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests: None declared.

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Authors' contributions: Conception and design (T.K., J.J.). Collection and assembly of data (J.H., J.J.). Data analysis and interpretation (T.K., J.H., J.J.). Writing manuscript (M.R., T.K., S.Y.P.) Final approval of manuscript (All authors). Accountable for all aspects of the work (All authors)

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Figure Legends

Figure 1. Flow chart of fracture case selection.

Figure 2. Summary characteristics of the number of fractures.

Figure 3. Generalized additive model for the effects of selected meteorological factors on hip fracture incidence. The bold line estimates the relative effect sizes for the hip fracture while the blue area estimates the 95% confidence intervals (Cis). The X-axis represents each selected meteorological factor. The Y-axis shows the relative effect size for the hip fracture. $PM_{2.5}$, particulate matter ≤2.5 μm.

Figure 4. Level of selected meteorological factors and adjusted excess risk for hip fracture: (a) average temperature, (b) daily rain, (c) wind speed, (d) daily snow, and (e) particulate matter ≤2.5 μm ($PM_{2.5}$). The Y-axes show the percentages of adjusted excess risk with 95% confidence intervals (Cis). *p<0.05.

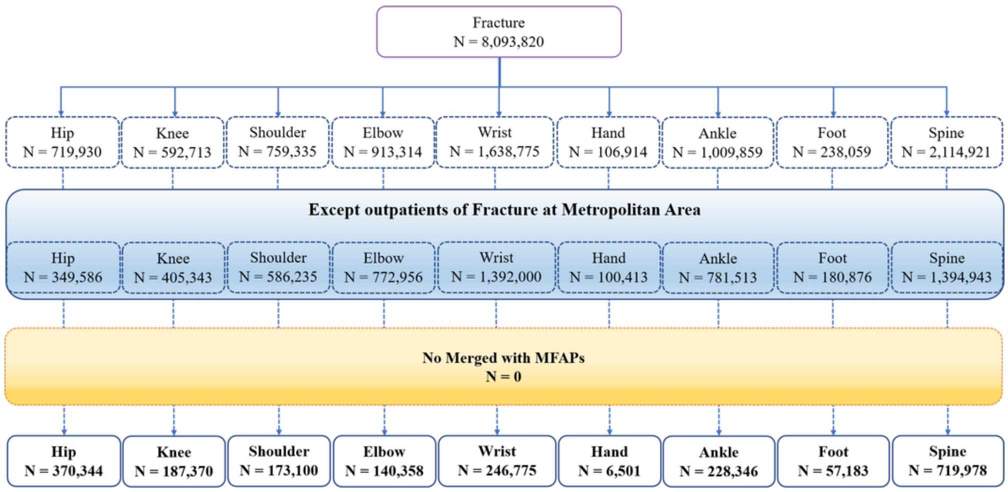

Figure 1. Flow chart of fracture case selection.

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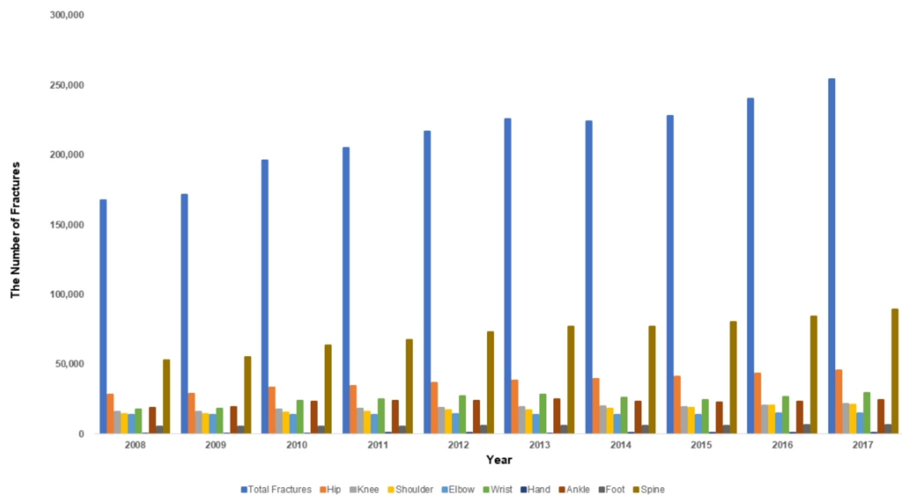


Figure 2. Summary characteristics of the number of fractures.

338x190mm (96 x 96 DPI)

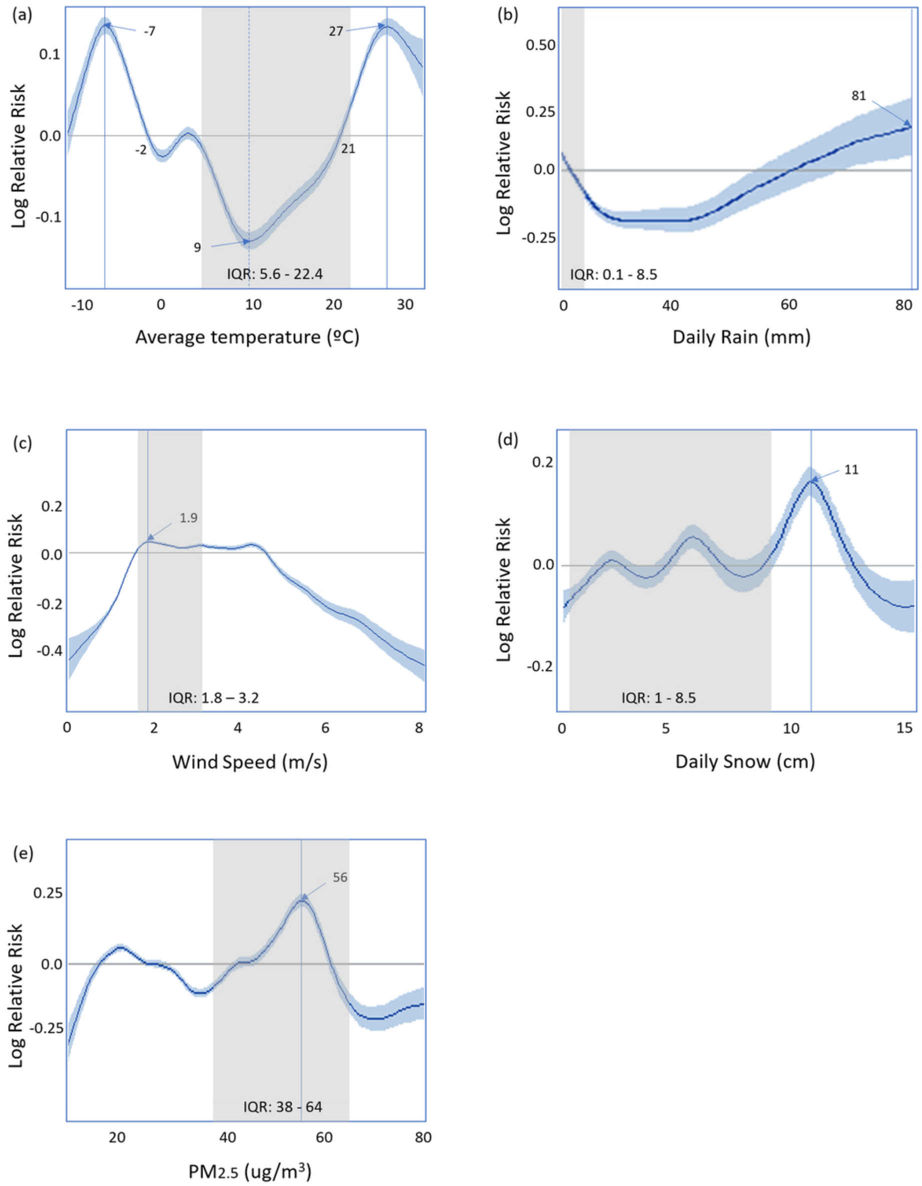


Figure 3. Generalized additive model for the effects of selected meteorological factors on hip fracture incidence. The bold line estimates the relative effect sizes for the hip fracture while the blue area estimates the 95% confidence intervals (Cis). The X-axis represents each selected meteorological factor. The Y-axis shows the relative effect size for the hip fracture. PM2.5, particulate matter ≤2.5 μm.

90x115mm (300 x 300 DPI)

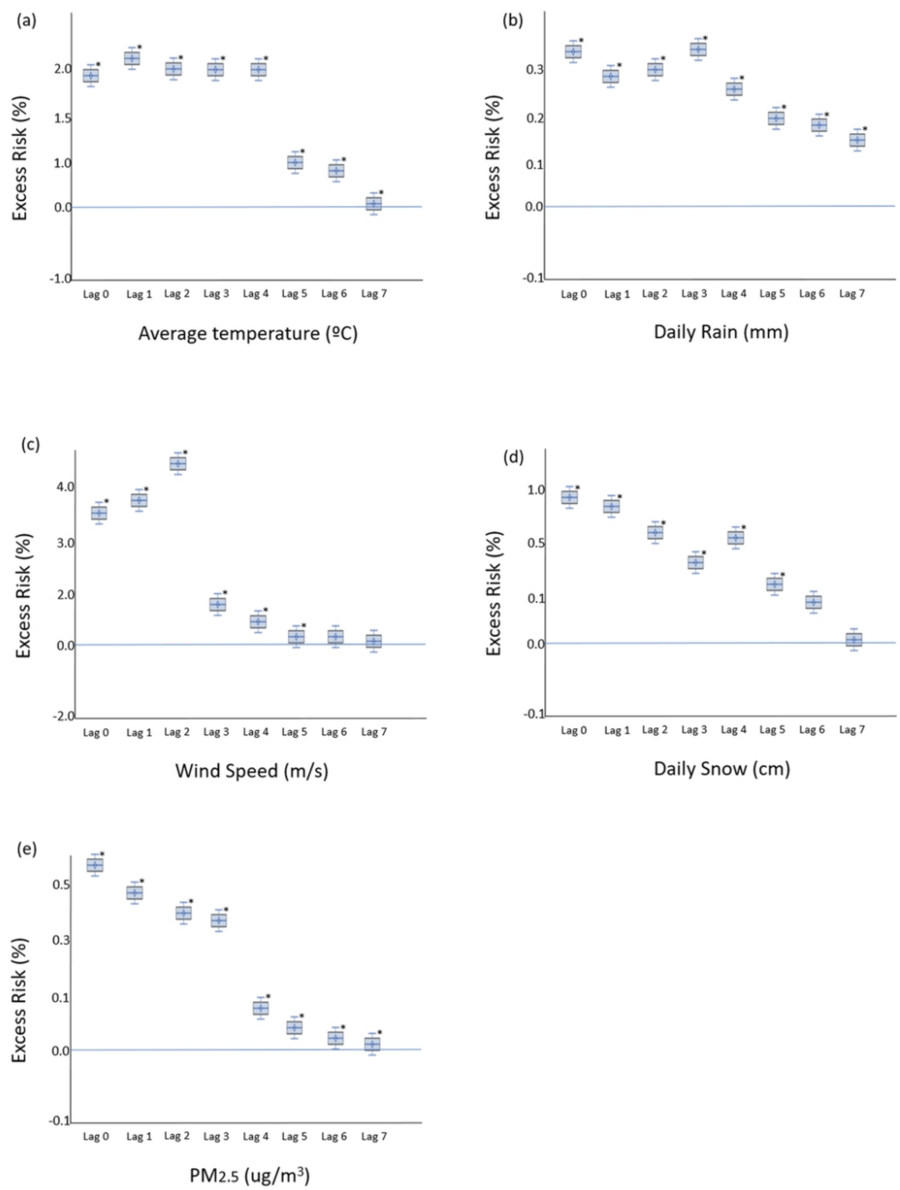


Figure 4. Level of selected meteorological factors and adjusted excess risk for hip fracture: (a) average temperature, (b) daily rain, (c) wind speed, (d) daily snow, and (e) particulate matter ≤2.5 μm (PM2.5). The Y-axes show the percentages of adjusted excess risk with 95% confidence intervals (Cis). *p<0.05.

90x119mm (300 x 300 DPI)

Online supplements

Supplemental Table 1. Data description on the meteorological factors and air pollution

Supplemental Table 2. Akaike Information Criterion (AIC) between site of fracture and meteorological factors including air pollutants (MFAPs)

Supplemental Table 3. Multivariate analysis of GAM with cubic splines for site of fracture depending on lags through from 2008 to 2017

Supplemental Figure 1. Generalized additive model for the effects of selected meteorological factors on the incidence of knee fracture

Supplemental Figure 2. Generalized additive model for the effects of selected meteorological factors on the incidence of shoulder fracture

Supplemental Figure 3. Generalized additive model for the effects of selected meteorological factors on the incidence of elbow fracture

Supplemental Figure 4. Generalized additive model for the effects of selected meteorological factors on the incidence of wrist fracture

Supplemental Figure 5. Generalized additive model for the effects of selected meteorological factors on the incidence of hand fracture

Supplemental Figure 6. Generalized additive model for the effects of selected meteorological factors on the incidence of ankle fracture

Supplemental Figure 7. Generalized additive model for the effects of selected meteorological factors on the incidence of foot fracture

Supplemental Figure 8. Generalized additive model for the effects of selected meteorological factors on the incidence of spine fracture

Supplemental Figure 9. Levels of the selected meteorological factors and adjusted excess risks of the knee fracture

Supplemental Figure 10. Levels of the selected meteorological factors and adjusted excess risks of the shoulder fracture

Supplemental Figure 11. Levels of the selected meteorological factors and adjusted excess risks of the elbow fracture

Supplemental Figure 12. Levels of the selected meteorological factors and adjusted excess risks of the wrist fracture

Supplemental Figure 13. Levels of the selected meteorological factors and adjusted excess risks of the hand fracture

Supplemental Figure 14. Levels of the selected meteorological factors and adjusted excess risks of the ankle fracture

Supplemental Figure 15. Levels of the selected meteorological factors and adjusted excess risks of the foot fracture

Supplemental Figure 16. Levels of the selected meteorological factors and adjusted excess risks of the spine fracture

Supplemental Table 1. Data description on the meteorological factors and air pollution

	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Meteorology (Mean, SD)										
Average Temperature (°C)	13.9(9.6)	13.9(9.4)	13.4(9.6)	12.8(9.4)	12.9(9.8)	13.6(9.6)	14.1(9.6)	14.0(9.4)	14.3(9.2)	14.0(9.3)
High Temperature (°C)	18.4(9.8)	18.4(9.6)	17.8(9.7)	17.2(9.5)	17.4(9.9)	18.1(9.7)	18.9(9.7)	18.9(9.6)	19.0(9.3)	18.8(9.3)
Low Temperature (°C)	10.1(9.7)	10.1(9.5)	9.8(10.9)	9.2(10.6)	9.1(11.0)	9.8(9.9)	10.2(9.9)	10.0(9.5)	10.3(9.4)	9.9(9.6)
Daily Range (°C)	8.3(2.9)	8.3(3.0)	7.9(2.9)	8.0(3.0)	8.3(2.7)	8.2(3.1)	8.6(3.1)	8.8(3.2)	8.7(2.9)	8.8(3.0)
Vapor Pressure (hPa)	11.9(7.8)	11.7(7.4)	12.5(8.9)	11.4(8.3)	11.3(8.3)	12.3(8.8)	12.9(8.4)	12.3(7.8)	12.9(8.8)	12.3(8.9)
Solar Radiation (MJ/m^2)	13.5(6.8)	13.8(7.1)	12.9(6.7)	13.1(6.9)	12.8(6.4)	13.0(6.8)	12.9(6.3)	13.1(6.6)	13.2(6.4)	13.7(6.9)
Sunshine Duration (hr)	12.2(1.7)	12.2(1.7)	12.2(1.7)	12.1(1.7)	12.2(1.7)	12.2(1.7)	12.2(1.7)	12.1(1.7)	12.2(1.7)	12.2(1.7)
Wind Speed (m/s)	2.4(0.9)	2.5(1.0)	2.5(1.0)	2.6(1.0)	2.7(1.0)	2.7(1.1)	2.5(1.0)	2.6(1.0)	2.4(1.0)	2.3(0.9)
Daily Rain (mm)	8.8(18.8)	13(31.5)	10(19.9)	12.8(31)	10.8(21)	9.5(18.1)	8.3(16.7)	6.1(10.6)	7.9(16.9)	6.2(16.3)
Dew Point Temperature (°C)	5.9(11.6)	5.8(11.2)	6.1(12.2)	4.6(12.5)	4.4(12.5)	5.8(12.1)	7.1(11.7)	6.8(10.6)	6.8(12.0)	5.8(12.3)
Humidity (%)	61(15.2)	61(15.8)	64(15.6)	60(16.9)	59(16.1)	62(16.1)	65(16.9)	65(16.2)	64(16.4)	61(16.1)
Daily snow (cm)	3.7(3.0)	2.4(2.2)	8.2(6.8)	2.7(2.1)	3.6(2.9)	5.5(4.3)	2.1(1.8)	2.4(2.5)	1.9(2.9)	1.9(1.6)
Cloud (1/10)	4.7(3.0)	4.6(3.1)	5.1(3.2)	5.0(3.3)	4.9(3.0)	4.8(3.1)	4.8(3.1)	4.8(3.1)	4.8(2.9)	4.6(3.0)
Air Pollutants (Mean, SD)										
$PM_{2.5}$ (ug/m^3)	-	-	-	-	28(12)	27(13)	25(14)	24(12)	25(14)	23(12)
PM_{10} (ug/m^3)	56(30)	54(29)	50(28)	49(30)	45(21)	47(23)	48(26)	47(34)	46(19)	45(20)
O_3 (100ppb)	1.9(0.9)	2.1(1.0)	1.9(0.9)	1.9(1.0)	2.1(1.0)	2.2(1.0)	2.3(1.1)	2.2(1.0)	2.4(1.1)	2.5(1.1)
NO_2 (100ppb)	3.4(1.4)	3.3(1.3)	3.2(1.3)	3.2(1.3)	3.1(1.2)	3.2(1.3)	3.1(1.3)	3.1(1.3)	2.9(1.1)	2.8(1.1)
SO_2 (100ppb)	0.6(0.2)	0.5(0.2)	0.5(0.2)	0.5(0.2)	0.5(0.2)	0.5(0.2)	0.5(0.2)	0.5(0.1)	0.4(0.1)	0.4(0.1)
CO (10ppm)	0.6(0.2)	0.6(0.2)	0.5(0.2)	0.5(0.2)	0.5(0.2)	0.5(0.2)	0.5(0.1)	0.5(0.1)	0.5(0.1)	0.4(0.1)

O_3 was analyzed by the 8-hour maximum per time or day.

SD denotes standard deviation; min, minimum; max, maximum; ppb, parts-per-billion; ppm, parts-per-million.

Supplemental Table 2.

Akaike Information Criterion (AIC) between site of fracture and meteorological factors including air pollutants (MFAPs)

Test	MFAP as effect	AIC
	Hip	
Test	MFAP as effect	AIC
1	Average Temperature, Diurnal Temperature Range, Daily Rain, Wind Speed, Dew point Temperature, Humidity, Vapor Pressure, Sunshine Duration, Solar Radiation, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, SO_2, O_3, NO_2	197.3
2	Average Temperature, Diurnal Temperature Range, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Sunshine Duration, Solar Radiation, Daily Snow, PM_{10}, $PM_{2.5}$, CO, O_3, NO_2	196.7
3	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Sunshine Duration, Solar Radiation, Daily Snow, PM_{10}, $PM_{2.5}$, CO, NO_2	196.2
4	Average Temperature, Daily Rain, Wind Speed, Vapor Pressure, Sunshine Duration, Solar Radiation, Daily Snow, PM_{10}, $PM_{2.5}$, CO,NO_2	191.7
5	Average Temperature, Daily Rain, Wind Speed, Vapor Pressure, Daily Snow, PM_{10}, $PM_{2.5}$, CO, NO_2	189.6
6	Average Temperature, Daily Rain, Wind Speed, Vapor Pressure, Daily Snow, PM_{10}, $PM_{2.5}$	188.5
7	Average Temperature, Daily Rain, Wind Speed, Daily Snow, PM_{10}, $PM_{2.5}$	188.5
8	**Average Temperature, Daily Rain, Wind Speed, Daily Snow, $PM_{2.5}$**	**187.3**
	Knee	
Test	MFAP as effect	AIC
1	Average Temperature, Diurnal Temperature Range, Daily Rain, Wind Speed, Dew point Temperature, Humidity, Vapor Pressure, Sunshine Duration, Solar Radiation, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, SO_2, O_3, NO_2	125.8
2	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Sunshine Duration, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, SO_2, O_3, NO_2	123.6
3	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Sunshine Duration, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, NO_2	123.1
4	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO	123.1
5	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Daily Snow, $PM_{2.5}$, CO	121.7
6	Average Temperature, Daily Rain, Wind Speed, Humidity, Daily Snow, $PM_{2.5}$, CO	121.7
7	**Average Temperature, Daily Rain, Wind Speed, Daily Snow, $PM_{2.5}$**	**119.5**
	Shoulder	
Test	MFAP as effect	AIC
1	Average Temperature, Diurnal Temperature Range, Daily Rain, Wind Speed, Dew point Temperature, Humidity, Vapor Pressure, Sunshine	151.1

	Duration, Solar Radiation, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, SO_2, O_3, NO_2	
2	Average Temperature, Diurnal Temperature Range, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Sunshine Duration, Solar Radiation, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, NO_2	149.9
3	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Sunshine Duration, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, NO_2	146.6
4	Average Temperature, Daily Rain, Wind Speed, Humidity, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, NO_2	146.3
5	Average Temperature, Daily Rain, Wind Speed, Humidity, Daily Snow, PM_{10}, $PM_{2.5}$	146.2
6	**Average Temperature, Daily Rain, Wind Speed, Daily Snow, $PM_{2.5}$**	**142.8**
	Elbow	
Test	MFAP as effect	AIC
1	Average Temperature, Diurnal Temperature Range, Daily Rain, Wind Speed, Dew point Temperature, Humidity, Vapor Pressure, Sunshine Duration, Solar Radiation, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, SO_2, O_3, NO_2	153.7
2	Average Temperature, Diurnal Temperature Range, Daily Rain, Wind Speed, Dew point Temperature, Vapor Pressure, Sunshine Duration, Solar Radiation, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, NO_2	153.5
3	Average Temperature, Daily Rain, Wind Speed, Dew point Temperature, Vapor Pressure, Sunshine Duration, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, NO_2	149.1
4	Average Temperature, Daily Rain, Wind Speed, Dew point Temperature, Vapor Pressure, Daily Snow, PM_{10}, $PM_{2.5}$, NO_2	148.2
5	Average Temperature, Daily Rain, Wind Speed, Daily Snow, PM_{10}, $PM_{2.5}$	148.1
6	**Average Temperature, Daily Rain, Wind Speed, Daily Snow, $PM_{2.5}$**	**145.8**
	Wrist	
Test	MFAP as effect	AIC
1	Average Temperature, Diurnal Temperature Range, Daily Rain, Wind Speed, Dew point Temperature, Humidity, Vapor Pressure, Sunshine Duration, Solar Radiation, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, SO_2, O_3, NO_2	480.2
2	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Sunshine Duration, Solar Radiation, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, O_3, NO_2	480.1
3	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Sunshine Duration, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO	477.8
4	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Daily Snow, PM_{10}, $PM_{2.5}$	473.4
5	Average Temperature, Daily Rain, Wind Speed, Daily Snow, PM_{10}, $PM_{2.5}$	469.6
6	**Average Temperature, Daily Rain, Wind Speed, Daily Snow, $PM_{2.5}$**	**460.5**
	Hand	
Test	MFAP as effect	AIC
1	Average Temperature, Diurnal Temperature Range, Daily Rain, Wind Speed, Dew point Temperature, Humidity, Vapor Pressure, Sunshine	1531.9

	Duration, Solar Radiation, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, SO_2, O_3, NO_2	
2	Average Temperature, Daily Rain, Wind Speed, Vapor Pressure, Sunshine Duration, Solar Radiation, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, SO_2, O_3, NO_2	1467.8
3	Average Temperature, Daily Rain, Wind Speed, Sunshine Duration, Solar Radiation, Daily Snow, Cloud, $PM_{2.5}$, CO, O_3, NO_2	1465.1
4	Average Temperature, Daily Rain, Wind Speed, Sunshine Duration, Daily Snow, $PM_{2.5}$, CO, NO_2	1455.3
5	Average Temperature, Daily Rain, Wind Speed, Daily Snow, $PM_{2.5}$, NO_2	1458.1
6	**Average Temperature, Daily Rain, Wind Speed, Daily Snow, $PM_{2.5}$**	**1452.4**
	Ankle	
Test	MFAP as effect	AIC
1	Average Temperature, Diurnal Temperature Range, Daily Rain, Wind Speed, Dew point Temperature, Humidity, Vapor Pressure, Sunshine Duration, Solar Radiation, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, SO_2, O_3, NO_2	237.1
2	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Sunshine Duration, Solar Radiation, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, SO_2, NO_2	235.7
3	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Sunshine Duration, Daily Snow, Cloud, $PM_{2.5}$, CO, NO_2	231.2
4	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Daily Snow, $PM_{2.5}$, NO_2	230.3
5	Average Temperature, Daily Rain, Wind Speed, Humidity, Daily Snow, $PM_{2.5}$	230.2
6	**Average Temperature, Daily Rain, Wind Speed, Daily Snow, $PM_{2.5}$**	**229.6**
	Foot	
Test	MFAP as effect	AIC
1	Average Temperature, Diurnal Temperature Range, Daily Rain, Wind Speed, Dew point Temperature, Humidity, Vapor Pressure, Sunshine Duration, Solar Radiation, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, SO_2, O_3, NO_2	299.2
2	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Sunshine Duration, Solar Radiation, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, SO_2, O_3, NO_2	290.8
3	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Sunshine Duration, Daily Snow, Cloud, $PM_{2.5}$, CO, SO_2, O_3, NO_2	290.5
4	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Sunshine Duration, Daily Snow, Cloud, $PM_{2.5}$, CO, NO_2	290.3
5	Average Temperature, Daily Rain, Wind Speed, Humidity, Daily Snow, Cloud, $PM_{2.5}$, CO, NO_2	289.8
6	Average Temperature, Daily Rain, Wind Speed, Daily Snow, $PM_{2.5}$, CO, NO_2	289.6
7	**Average Temperature, Daily Rain, Wind Speed, Daily Snow, $PM_{2.5}$**	**289.1**
	Spine	
Test	MFAP as effect	AIC
1	Average Temperature, Diurnal Temperature Range, Daily Rain, Wind Speed, Dew point Temperature, Humidity, Vapor Pressure, Sunshine	434.1

	Duration, Solar Radiation, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, SO_2, O_3, NO_2	
2	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Sunshine Duration, Solar Radiation, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, SO_2, O_3, NO_2	429.2
3	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Sunshine Duration, Daily Snow, Cloud, PM_{10}, $PM_{2.5}$, CO, SO_2, NO_2	425.6
4	Average Temperature, Daily Rain, Wind Speed, Humidity, Vapor Pressure, Sunshine Duration, Daily Snow, PM_{10}, $PM_{2.5}$, CO, NO_2	425.1
5	Average Temperature, Daily Rain, Wind Speed, Humidity, Daily Snow, PM_{10}, $PM_{2.5}$, CO, NO_2	424.7
6	Average Temperature, Daily Rain, Wind Speed, Humidity, Daily Snow, $PM_{2.5}$, CO	424.5
7	**Average Temperature, Daily Rain, Wind Speed, Humidity, Daily Snow, $PM_{2.5}$**	**422.1**

Supplemental Table 3.

Multivariate analysis of GAM with cubic splines for site of fracture depending on lags through from 2008 to 2017

Time	Variables	Hip				Knee			
		RR	ER(%)	95% CI	P-value	RR	ER(%)	95% CI	P-value
Lag 0	Avg. Temp.	1.0199	1.99	[1.0196-1.0202]	<.0001	1.0162	1.62	[1.0159-1.0165]	<.0001
	Daily Rain	1.0033	0.33	[1.0030-1.0036]	<.0001	1.0021	0.21	[1.0018-1.0024]	<.0001
	Wind Speed	1.0354	3.54	[1.0324-1.0383]	<.0001	1.0242	2.42	[1.0210-1.0275]	<.0001
	Daily Snow	1.0099	0.99	[1.0081-1.0117]	<.0001	1.0116	1.16	[1.0097-1.0135]	<.0001
	$PM_{2.5}$	1.0055	0.55	[1.0052-1.0057]	<.0001	1.0037	0.37	[1.0034-1.0040]	<.0001
Lag 1	Avg. Temp.	1.0202	2.02	[1.0199-1.0204]	<.0001	1.0163	1.63	[1.0161-1.0166]	<.0001
	Daily Rain	1.0029	0.29	[1.0027-1.0031]	<.0001	1.0015	0.15	[1.0013-1.0017]	<.0001
	Wind Speed	1.0379	3.79	[1.0359-1.0399]	<.0001	1.0298	2.98	[1.0274-1.0323]	<.0001
	Daily Snow	1.0083	0.83	[1.0070-1.0096]	0.0003	1.0115	1.15	[1.0100-1.0129]	<.0001
	$PM_{2.5}$	1.0048	0.48	[1.0046-1.0050]	<.0001	1.0037	0.37	[1.0035-1.0040]	<.0001
Lag 2	Avg. Temp.	1.0200	2.00	[1.0198-1.0203]	<.0001	1.0163	1.63	[1.0161-1.0166]	<.0001
	Daily Rain	1.0030	0.30	[1.0028-1.0032]	0.0002	1.0017	0.17	[1.0015-1.0019]	<.0001
	Wind Speed	1.0442	4.42	[1.0422-1.0462]	<.0001	1.0343	3.43	[1.0319-1.0367]	<.0001
	Daily Snow	1.0058	0.58	[1.0045-1.0071]	<.0001	1.0099	0.99	[1.0085-1.0114]	<.0001
	$PM_{2.5}$	1.0039	0.39	[1.0037-1.0041]	<.0001	1.0029	0.29	[1.0027-1.0032]	0.0005
Lag 3	Avg. Temp.	1.0200	2.00	[1.0198-1.0202]	<.0001	1.0163	1.63	[1.0161-1.0165]	<.0001
	Daily Rain	1.0034	0.34	[1.0032-1.0036]	0.0001	1.0018	0.18	[1.0015-1.0020]	0.0002
	Wind Speed	1.0180	1.80	[1.0158-1.0201]	<.0001	1.0286	2.86	[1.0262-1.0310]	<.0001
	Daily Snow	1.0036	0.36	[1.0023-1.0050]	0.0004	1.0058	0.58	[1.0043-1.0074]	<.0001
	$PM_{2.5}$	1.0034	0.34	[1.0032-1.0037]	<.0001	1.0031	0.31	[1.0028-1.0034]	<.0001
Lag 4	Avg. Temp.	1.0200	2.00	[1.0198-1.0202]	<.0001	1.0162	1.62	[1.0159-1.0164]	<.0001
	Daily Rain	1.0026	0.26	[1.0024-1.0028]	0.0002	1.0020	0.20	[1.0017-1.0022]	0.0005
	Wind Speed	1.0096	0.96	[1.0075-1.0118]	<.0001	1.0229	2.29	[1.0204-1.0254]	<.0001
	Daily Snow	1.0052	0.52	[1.0039-1.0066]	<.0001	1.0026	0.26	[1.0010-1.0042]	<.0001
	$PM_{2.5}$	1.0009	0.09	[1.0007-1.0012]	0.0512	1.0024	0.24	[1.0021-1.0026]	<.0001
Lag 5	Avg. Temp.	1.0101	1.01	[1.0099-1.0103]	<.0001	1.0163	1.63	[1.0161-1.0165]	<.0001

	Daily Rain	1.0020	0.20	[1.0018-1.0022]	0.0001	1.0017	0.17	[1.0015-1.0020]	<.0001
	Wind Speed	1.0023	0.23	[1.0001-1.0044]	0.0432	1.0204	2.04	[1.0179-1.0229]	<.0001
	Daily Snow	1.0018	0.18	[1.0003-1.0032]	<.0001	1.0024	0.24	[1.0007-1.0041]	0.0218
	$PM_{2.5}$	1.0006	0.06	[1.0003-1.0008]	<.0001	1.0019	0.19	[1.0017-1.0022]	<.0001
Lag 6	Avg. Temp.	1.0099	0.99	[1.0097-1.0101]	<.0001	1.0163	1.63	[1.0160-1.0165]	<.0001
	Daily Rain	1.0019	0.19	[1.0017-1.0021]	0.0002	1.0016	0.16	[1.0014-1.0018]	<.0001
	Wind Speed	1.0020	0.20	[0.9998-1.0041]	0.4289	1.0103	1.03	[1.0079-1.0128]	<.0001
	Daily Snow	1.0011	0.11	[0.9996-1.0025]	0.5743	1.0007	0.07	[0.9990-1.0023]	0.1976
	$PM_{2.5}$	1.0004	0.04	[1.0002-1.0006]	0.0012	1.0014	0.14	[1.0011-1.0017]	<.0001
Lag 7	Avg. Temp.	1.0020	0.20	[1.0018-1.0022]	0.0023	1.0163	1.63	[1.0161-1.0165]	<.0001
	Daily Rain	1.0016	0.16	[1.0014-1.0018]	0.0005	1.0009	0.09	[1.0006-1.0011]	0.0356
	Wind Speed	1.0014	0.14	[0.9993-1.0034]	0.4980	1.0024	0.24	[0.9999-1.0048]	0.5569
	Daily Snow	1.0009	0.09	[0.9995-1.0023]	0.5533	1.0003	0.03	[0.9988-1.0019]	0.7635
	$PM_{2.5}$	1.0003	0.03	[1.0001-1.0005]	0.0045	1.0009	0.09	[1.0006-1.0012]	0.0144

Time	Variables	Shoulder				Elbow			
		RR	ER(%)	95% CI	P-value	RR	ER(%)	95% CI	P-value
Lag 0	Avg. Temp.	1.0134	1.34	[1.0131-1.0137]	<.0001	1.0101	1.01	[1.0099-1.0104]	<.0001
	Daily Rain	1.0015	0.15	[1.0012-1.0018]	<.0001	1.0015	0.15	[1.0012-1.0018]	<.0001
	Wind Speed	1.0165	1.65	[1.0134-1.0197]	<.0001	1.0124	1.24	[1.0093-1.0155]	<.0001
	Daily Snow	1.0128	1.28	[1.0110-1.0146]	<.0001	1.0149	1.49	[1.0132-1.0166]	<.0001
	$PM_{2.5}$	1.0032	0.32	[1.0029-1.0035]	<.0001	1.0019	0.19	[1.0016-1.0023]	<.0001
Lag 1	Avg. Temp.	1.0136	1.36	[1.0134-1.0138]	<.0001	1.0103	1.03	[1.0101-1.0105]	<.0001
	Daily Rain	1.0013	0.13	[1.0012-1.0015]	<.0001	1.0008	0.08	[1.0006-1.0010]	0.0013
	Wind Speed	1.0209	2.09	[1.0189-1.0230]	<.0001	1.0178	1.78	[1.0159-1.0196]	<.0001
	Daily Snow	1.0130	1.30	[1.0118-1.0142]	<.0001	1.0144	1.44	[1.0134-1.0155]	<.0001
	$PM_{2.5}$	1.0033	0.33	[1.0031-1.0035]	<.0001	1.0020	0.20	[1.0018-1.0022]	<.0001
Lag 2	Avg. Temp.	1.0135	1.35	[1.0133-1.0137]	<.0001	1.0104	1.04	[1.0102-1.0105]	<.0001
	Daily Rain	1.0014	0.14	[1.0012-1.0016]	<.0001	1.0008	0.08	[1.0006-1.0009]	0.0017
	Wind Speed	1.0255	2.55	[1.0234-1.0275]	<.0001	1.0201	2.01	[1.0182-1.0219]	<.0001
	Daily Snow	1.0112	1.12	[1.0099-1.0124]	<.0001	1.0116	1.16	[1.0105-1.0126]	<.0001
	$PM_{2.5}$	1.0034	0.34	[1.0031-1.0036]	<.0001	1.0021	0.21	[1.0019-1.0023]	0.0005

Lag 3	Avg. Temp.	1.0135	1.35	[1.0133-1.0137]	<.0001	1.0103	1.03	[1.0101-1.0105]	<.0001
	Daily Rain	1.0012	0.12	[1.0010-1.0013]	0.0006	1.0009	0.09	[1.0007-1.0010]	0.0018
	Wind Speed	1.0218	2.18	[1.0198-1.0239]	<.0001	1.0248	2.48	[1.0230-1.0266]	<.0001
	Daily Snow	1.0075	0.75	[1.0062-1.0088]	<.0001	1.0097	0.97	[1.0086-1.0108]	<.0001
	$PM_{2.5}$	1.0033	0.33	[1.0030-1.0035]	<.0001	1.0019	0.19	[1.0017-1.0021]	<.0001
Lag 4	Avg. Temp.	1.0135	1.35	[1.0133-1.0137]	<.0001	1.0101	1.01	[1.0099-1.0103]	<.0001
	Daily Rain	1.0014	0.14	[1.0012-1.0016]	<.0001	1.0010	0.10	[1.0009-1.0012]	<.0001
	Wind Speed	1.0181	1.81	[1.0160-1.0201]	<.0001	1.0188	1.88	[1.0170-1.0207]	<.0001
	Daily Snow	1.0028	0.28	[1.0015-1.0042]	<.0001	1.0070	0.70	[1.0059-1.0082]	<.0001
	$PM_{2.5}$	1.0023	0.23	[1.0021-1.0026]	<.0001	1.0017	0.17	[1.0015-1.0019]	<.0001
Lag 5	Avg. Temp.	1.0137	1.37	[1.0135-1.0138]	<.0001	1.0102	1.02	[1.0101-1.0104]	<.0001
	Daily Rain	1.0014	0.14	[1.0012-1.0015]	0.0001	1.0009	0.09	[1.0007-1.0010]	0.0011
	Wind Speed	1.0173	1.73	[1.0152-1.0194]	<.0001	1.0172	1.72	[1.0153-1.0190]	<.0001
	Daily Snow	1.0002	0.02	[0.9988-1.0017]	0.1489	1.0013	0.13	[1.0000-1.0025]	0.0561
	$PM_{2.5}$	1.0017	0.17	[1.0015-1.0020]	<.0001	1.0010	0.10	[1.0008-1.0013]	0.0023
Lag 6	Avg. Temp.	1.0136	1.36	[1.0134-1.0138]	<.0001	1.0103	1.03	[1.0101-1.0105]	<.0001
	Daily Rain	1.0008	0.08	[1.0007-1.0010]	0.0028	1.0009	0.09	[1.0007-1.0010]	0.0013
	Wind Speed	1.0149	1.49	[1.0129-1.0170]	<.0001	1.0153	1.53	[1.0135-1.0171]	<.0001
	Daily Snow	1.0001	0.01	[0.9987-1.0015]	0.5731	1.0012	0.12	[0.9999-1.0024]	0.4791
	$PM_{2.5}$	1.0012	0.12	[1.0010-1.0015]	0.0010	1.0009	0.09	[1.0007-1.0011]	0.0031
Lag 7	Avg. Temp.	1.0137	1.37	[1.0135-1.0139]	<.0001	1.0103	1.03	[1.0102-1.0105]	<.0001
	Daily Rain	1.0001	0.01	[1.0000-1.0003]	0.0556	1.0007	0.07	[1.0005-1.0008]	0.0033
	Wind Speed	1.0111	1.11	[1.0090-1.0131]	<.0001	1.0119	1.19	[1.0100-1.0137]	0.5569
	Daily Snow	1.0001	0.01	[0.9988-1.0015]	0.7631	1.0009	0.09	[0.9997-1.0021]	0.6583
	$PM_{2.5}$	1.0003	0.03	[1.0000-1.0005]	0.0612	1.0008	0.08	[1.0006-1.0010]	0.0237
Time	Variables	Wrist				Hand			
		RR	ER(%)	95% CI	P-value	RR	ER(%)	95% CI	P-value
Lag 0	Avg. Temp.	1.0148	1.48	[1.0146-1.0151]	<.0001	1.0203	2.03	[1.0195-1.0211]	<.0001
	Daily Rain	1.0023	0.23	[1.0020-1.0025]	<.0001	1.0025	0.25	[1.0016-1.0033]	<.0001
	Wind Speed	1.0174	1.74	[1.0147-1.0201]	<.0001	1.0058	0.58	[0.9959-1.0157]	<.0001
	Daily Snow	1.0145	1.45	[1.0133-1.0158]	<.0001	1.0241	2.41	[1.0196-1.0285]	<.0001

	$PM_{2.5}$	1.0020	0.20	[1.0017-1.0023]	<.0001	1.0047	0.47	[1.0038-1.0056]	<.0001
Lag 1	Avg. Temp.	1.0149	1.49	[1.0148-1.0150]	<.0001	1.0205	2.05	[1.0196-1.0213]	<.0001
	Daily Rain	1.0020	0.20	[1.0019-1.0022]	<.0001	1.0027	0.27	[1.0019-1.0035]	0.0013
	Wind Speed	1.0218	2.18	[1.0206-1.0230]	<.0001	1.0157	1.57	[1.0061-1.0254]	<.0001
	Daily Snow	1.0143	1.43	[1.0137-1.0148]	<.0001	1.0237	2.37	[1.0188-1.0285]	<.0001
	$PM_{2.5}$	1.0022	0.22	[1.0020-1.0023]	<.0001	1.0043	0.43	[1.0033-1.0052]	<.0001
Lag 2	Avg. Temp.	1.0149	1.49	[1.0148-1.0151]	<.0001	1.0207	2.07	[1.0198-1.0215]	<.0001
	Daily Rain	1.0020	0.20	[1.0019-1.0021]	<.0001	1.0014	0.14	[1.0006-1.0021]	0.0024
	Wind Speed	1.0238	2.38	[1.0226-1.0250]	<.0001	1.0237	2.37	[1.0141-1.0332]	<.0001
	Daily Snow	1.0116	1.16	[1.0110-1.0122]	<.0001	1.0172	1.72	[1.0122-1.0223]	<.0001
	$PM_{2.5}$	1.0021	0.21	[1.0019-1.0022]	<.0001	1.0041	0.41	[1.0031-1.0050]	<.0001
Lag 3	Avg. Temp.	1.0149	1.49	[1.0147-1.0150]	<.0001	1.0207	2.07	[1.0199-1.0215]	<.0001
	Daily Rain	1.0018	0.18	[1.0017-1.0019]	<.0001	1.0019	0.19	[1.0012-1.0027]	<.0001
	Wind Speed	1.0282	2.82	[1.0270-1.0293]	<.0001	1.0308	3.08	[1.0214-1.0402]	<.0001
	Daily Snow	1.0099	0.99	[1.0093-1.0105]	<.0001	1.0112	1.12	[1.0060-1.0165]	<.0001
	$PM_{2.5}$	1.0025	0.25	[1.0023-1.0026]	<.0001	1.0049	0.49	[1.0039-1.0058]	<.0001
Lag 4	Avg. Temp.	1.0146	1.46	[1.0145-1.0147]	<.0001	1.0205	2.05	[1.0197-1.0213]	<.0001
	Daily Rain	1.0019	0.19	[1.0018-1.0020]	<.0001	1.0032	0.32	[1.0023-1.0041]	<.0001
	Wind Speed	1.0197	1.97	[1.0185-1.0209]	<.0001	1.0335	3.35	[1.0240-1.0430]	<.0001
	Daily Snow	1.0078	0.78	[1.0071-1.0084]	<.0001	1.0083	0.83	[1.0031-1.0135]	<.0001
	$PM_{2.5}$	1.0025	0.25	[1.0023-1.0026]	<.0001	1.0039	0.39	[1.0030-1.0049]	<.0001
Lag 5	Avg. Temp.	1.0146	1.46	[1.0145-1.0147]	<.0001	1.0205	2.05	[1.0197-1.0213]	<.0001
	Daily Rain	1.0017	0.17	[1.0015-1.0018]	<.0001	1.0022	0.22	[1.0015-1.0030]	<.0001
	Wind Speed	1.0173	1.73	[1.0161-1.0185]	<.0001	1.0340	3.40	[1.0245-1.0434]	<.0001
	Daily Snow	1.0030	0.30	[1.0024-1.0037]	<.0001	1.0017	0.17	[0.9961-1.0073]	0.1469
	$PM_{2.5}$	1.0012	0.12	[1.0011-1.0014]	<.0001	1.0021	0.21	[1.0010-1.0031]	<.0001
Lag 6	Avg. Temp.	1.0146	1.46	[1.0145-1.0147]	<.0001	1.0206	2.06	[1.0198-1.0215]	<.0001
	Daily Rain	1.0014	0.14	[1.0013-1.0015]	<.0001	1.0006	0.06	[0.9999-1.0012]	0.8631
	Wind Speed	1.0124	1.24	[1.0112-1.0136]	<.0001	1.0184	1.84	[1.0090-1.0278]	<.0001
	Daily Snow	1.0026	0.26	[1.0020-1.0033]	<.0001	1.0010	0.10	[0.9954-1.0066]	0.7764
	$PM_{2.5}$	1.0010	0.10	[1.0009-1.0012]	0.0009	1.0012	0.12	[1.0002-1.0022]	0.0035

Lag 7	Avg. Temp.	1.0146	1.46	[1.0145-1.0147]	<.0001	1.0205	2.05	[1.0197-1.0214]	<.0001
	Daily Rain	1.0009	0.09	[1.0007-1.0010]	0.0004	1.0002	0.02	[0.9994-1.0011]	0.7490
	Wind Speed	1.0106	1.06	[1.0094-1.0118]	<.0001	1.0024	0.24	[0.9929-1.0118]	0.6931
	Daily Snow	1.0014	0.14	[1.0007-1.0020]	0.0012	1.0003	0.03	[0.9949-1.0057]	0.6132
	$PM_{2.5}$	1.0008	0.08	[1.0007-1.0010]	0.0011	1.0008	0.08	[0.9998-1.0018]	0.3885

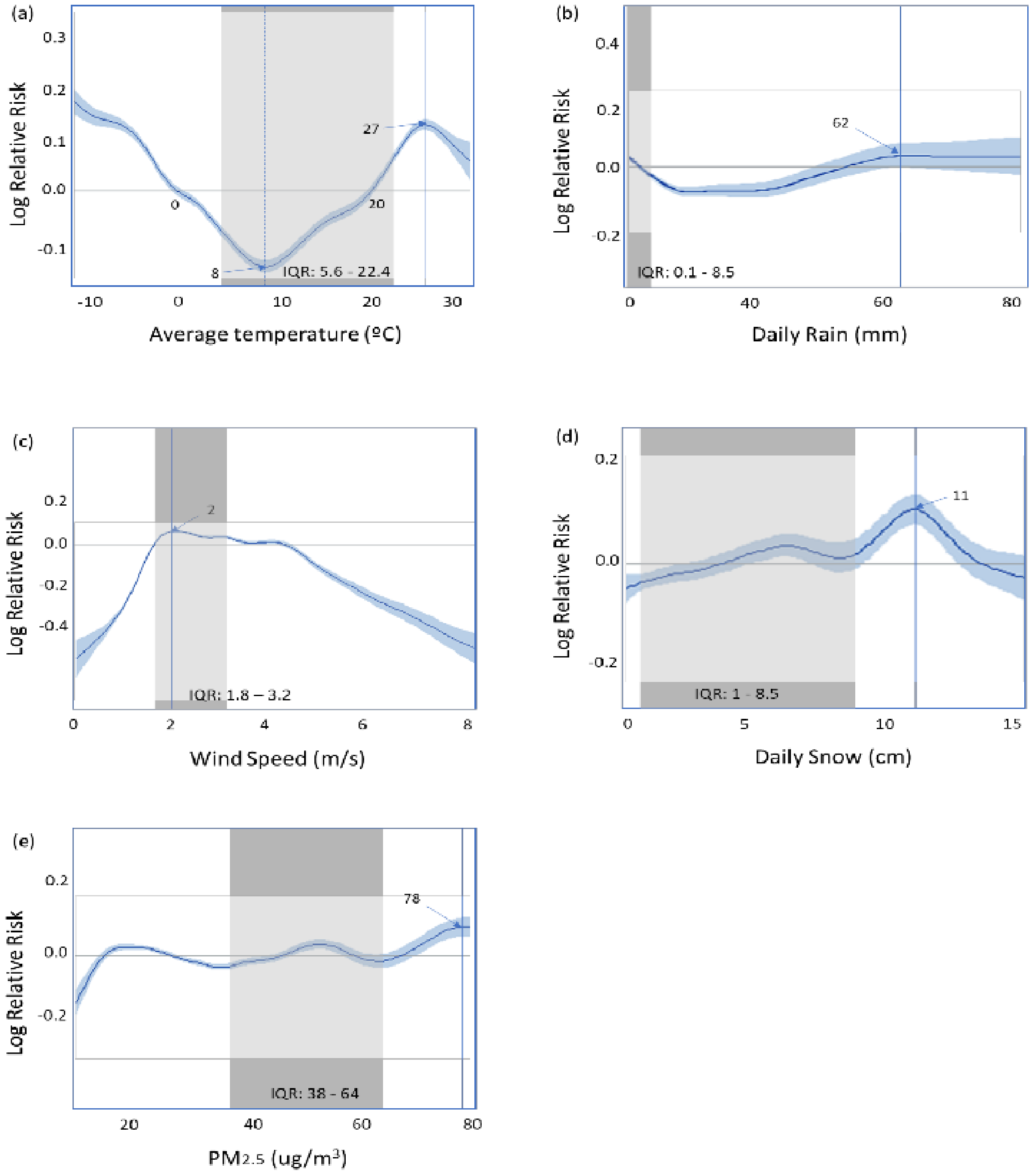
Time	Variables	**Ankle**				**Foot**			
		RR	ER(%)	95% CI	P-value	RR	ER(%)	95% CI	P-value
Lag 0	Avg. Temp.	1.0144	1.44	[1.0141-1.0146]	<.0001	1.0122	1.22	[1.0117-1.0126]	<.0001
	Daily Rain	1.0018	0.18	[1.0015-1.0021]	<.0001	1.0020	0.20	[1.0015-1.0025]	<.0001
	Wind Speed	1.0210	2.10	[1.0181-1.0239]	<.0001	1.0265	2.65	[1.0215-1.0315]	<.0001
	Daily Snow	1.0115	1.15	[1.0100-1.0131]	<.0001	1.0197	1.97	[1.0166-1.0228]	<.0001
	$PM_{2.5}$	1.0026	0.26	[1.0023-1.0029]	<.0001	1.0041	0.41	[1.0036-1.0046]	<.0001
Lag 1	Avg. Temp.	1.0144	1.44	[1.0143-1.0146]	<.0001	1.0122	1.22	[1.0118-1.0127]	<.0001
	Daily Rain	1.0015	0.15	[1.0013-1.0016]	<.0001	1.0009	0.09	[1.0004-1.0013]	0.0022
	Wind Speed	1.0257	2.57	[1.0241-1.0273]	<.0001	1.0358	3.58	[1.0309-1.0407]	<.0001
	Daily Snow	1.0119	1.19	[1.0110-1.0128]	<.0001	1.0199	1.99	[1.0168-1.0229]	<.0001
	$PM_{2.5}$	1.0027	0.27	[1.0026-1.0029]	<.0001	1.0044	0.44	[1.0039-1.0049]	<.0001
Lag 2	Avg. Temp.	1.0144	1.44	[1.0143-1.0146]	<.0001	1.0123	1.23	[1.0118-1.0127]	<.0001
	Daily Rain	1.0017	0.17	[1.0016-1.0019]	<.0001	1.0012	0.12	[1.0008-1.0016]	0.0031
	Wind Speed	1.0280	2.80	[1.0264-1.0296]	<.0001	1.0360	3.60	[1.0312-1.0409]	<.0001
	Daily Snow	1.0105	1.05	[1.0096-1.0114]	<.0001	1.0124	1.24	[1.0091-1.0158]	<.0001
	$PM_{2.5}$	1.0030	0.30	[1.0028-1.0032]	<.0001	1.0037	0.37	[1.0032-1.0042]	<.0001
Lag 3	Avg. Temp.	1.0143	1.43	[1.0141-1.0145]	<.0001	1.0122	1.22	[1.0118-1.0127]	<.0001
	Daily Rain	1.0016	0.16	[1.0014-1.0017]	<.0001	1.0010	0.10	[1.0006-1.0014]	0.0032
	Wind Speed	1.0280	2.80	[1.0264-1.0296]	<.0001	1.0350	3.50	[1.0301-1.0399]	<.0001
	Daily Snow	1.0079	0.79	[1.0070-1.0089]	<.0001	1.0069	0.69	[1.0034-1.0104]	<.0001
	$PM_{2.5}$	1.0032	0.32	[1.0030-1.0034]	<.0001	1.0032	0.32	[1.0027-1.0038]	<.0001
Lag 4	Avg. Temp.	1.0142	1.42	[1.0140-1.0143]	<.0001	1.0122	1.22	[1.0117-1.0127]	<.0001
	Daily Rain	1.0020	0.20	[1.0019-1.0022]	<.0001	1.0015	0.15	[1.0010-1.0019]	<.0001
	Wind Speed	1.0207	2.07	[1.0190-1.0223]	<.0001	1.0303	3.03	[1.0254-1.0352]	<.0001
	Daily Snow	1.0058	0.58	[1.0048-1.0067]	<.0001	1.0007	0.07	[0.9971-1.0044]	0.4638

	$PM_{2.5}$	1.0027	0.27	[1.0025-1.0029]	<.0001	1.0017	0.17	[1.0012-1.0023]	<.0001
Lag 5	Avg. Temp.	1.0144	1.44	[1.0143-1.0146]	<.0001	1.0123	1.23	[1.0119-1.0128]	<.0001
	Daily Rain	1.0019	0.19	[1.0018-1.0021]	<.0001	1.0012	0.12	[1.0008-1.0016]	0.0029
	Wind Speed	1.0200	2.00	[1.0183-1.0216]	<.0001	1.0248	2.48	[1.0198-1.0297]	<.0001
	Daily Snow	1.0016	0.16	[1.0006-1.0027]	0.0004	1.0013	0.13	[0.9971-1.0055]	0.3975
	$PM_{2.5}$	1.0019	0.19	[1.0017-1.0021]	<.0001	1.0013	0.13	[1.0008-1.0019]	<.0001
Lag 6	Avg. Temp.	1.0145	1.45	[1.0144-1.0147]	<.0001	1.0126	1.26	[1.0121-1.0130]	<.0001
	Daily Rain	1.0016	0.16	[1.0015-1.0017]	<.0001	1.0006	0.06	[1.0002-1.0010]	0.0015
	Wind Speed	1.0189	1.89	[1.0173-1.0205]	<.0001	1.0230	2.30	[1.0181-1.0279]	<.0001
	Daily Snow	1.0011	0.11	[1.0001-1.0022]	0.0010	1.0011	0.11	[0.9970-1.0053]	0.6470
	$PM_{2.5}$	1.0014	0.14	[1.0012-1.0015]	<.0001	1.0011	0.11	[1.0006-1.0017]	0.0041
Lag 7	Avg. Temp.	1.0146	1.46	[1.0144-1.0147]	<.0001	1.0127	1.27	[1.0122-1.0131]	<.0001
	Daily Rain	1.0011	0.11	[1.0010-1.0013]	<.0001	1.0004	0.04	[1.0000-1.0008]	0.0673
	Wind Speed	1.0156	1.56	[1.0139-1.0172]	<.0001	1.0137	1.37	[1.0088-1.0186]	<.0001
	Daily Snow	1.0008	0.08	[0.9998-1.0018]	0.7763	1.0008	0.08	[0.9969-1.0047]	0.5796
	$PM_{2.5}$	1.0005	0.05	[1.0003-1.0006]	0.0015	1.0001	0.01	[0.9995-1.0006]	0.4159

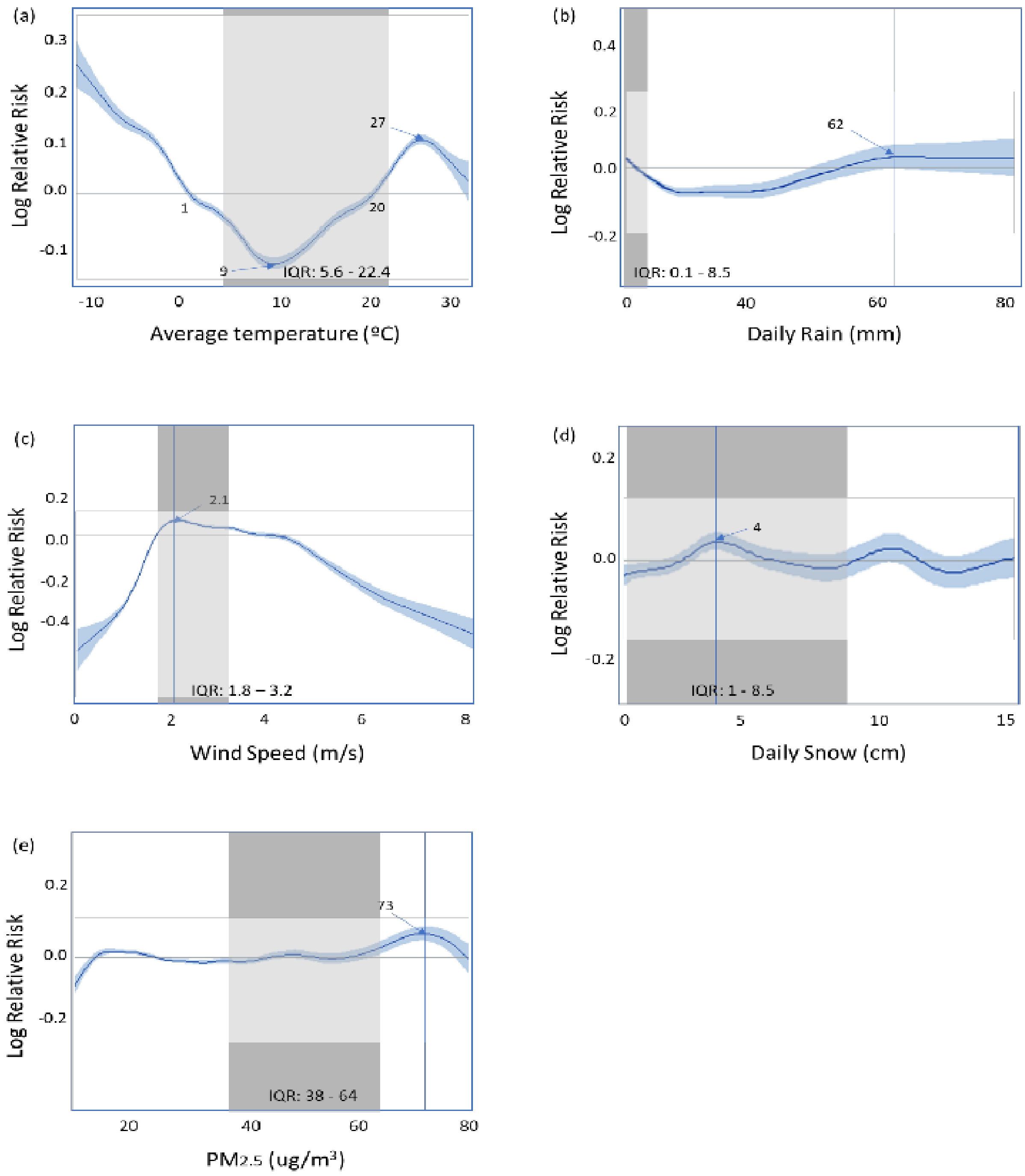
Time	Variables	Spine			
		RR	ER(%)	95% CI	P-value
Lag 0	Avg. Temp.	1.0101	1.01	[1.0099-1.0104]	<.0001
	Daily Rain	1.0010	0.10	[1.0007-1.0012]	<.0001
	Wind Speed	1.0209	2.09	[1.0183-1.0234]	<.0001
	Daily Snow	1.0087	0.87	[1.0069-1.0105]	<.0001
	$PM_{2.5}$	1.0025	0.25	[1.0022-1.0027]	<.0001
Lag 1	Avg. Temp.	1.0101	1.01	[1.0100-1.0102]	<.0001
	Daily Rain	1.0007	0.07	[1.0006-1.0008]	<.0001
	Wind Speed	1.0214	2.14	[1.0203-1.0225]	<.0001
	Daily Snow	1.0085	0.85	[1.0078-1.0093]	<.0001
	$PM_{2.5}$	1.0025	0.25	[1.0024-1.0026]	<.0001
Lag 2	Avg. Temp.	1.0102	1.02	[1.0101-1.0103]	<.0001
	Daily Rain	1.0008	0.08	[1.0007-1.0008]	<.0001
	Wind Speed	1.0234	2.34	[1.0223-1.0245]	<.0001

	Daily Snow	1.0077	0.77	[1.0070-1.0085]	<.0001
	$PM_{2.5}$	1.0021	0.21	[1.0020-1.0023]	<.0001
Lag 3	Avg. Temp.	1.0102	1.02	[1.0101-1.0103]	<.0001
	Daily Rain	1.0008	0.08	[1.0007-1.0009]	<.0001
	Wind Speed	1.0230	2.30	[1.0220-1.0241]	<.0001
	Daily Snow	1.0056	0.56	[1.0048-1.0063]	<.0001
	$PM_{2.5}$	1.0020	0.20	[1.0019-1.0021]	<.0001
Lag 4	Avg. Temp.	1.0102	1.02	[1.0101-1.0103]	<.0001
	Daily Rain	1.0009	0.09	[1.0008-1.0010]	<.0001
	Wind Speed	1.0205	2.05	[1.0194-1.0216]	<.0001
	Daily Snow	1.0046	0.46	[1.0038-1.0054]	<.0001
	$PM_{2.5}$	1.0016	0.16	[1.0015-1.0017]	<.0001
Lag 5	Avg. Temp.	1.0103	1.03	[1.0102-1.0104]	<.0001
	Daily Rain	1.0009	0.09	[1.0008-1.0010]	<.0001
	Wind Speed	1.0176	1.76	[1.0165-1.0187]	<.0001
	Daily Snow	1.0005	0.05	[0.9996-1.0013]	0.6304
	$PM_{2.5}$	1.0015	0.15	[1.0014-1.0016]	<.0001
Lag 6	Avg. Temp.	1.0103	1.03	[1.0101-1.0104]	<.0001
	Daily Rain	1.0008	0.08	[1.0007-1.0009]	<.0001
	Wind Speed	1.0105	1.05	[1.0094-1.0116]	<.0001
	Daily Snow	1.0003	0.03	[0.9995-1.0012]	0.7136
	$PM_{2.5}$	1.0012	0.12	[1.0011-1.0014]	<.0001
Lag 7	Avg. Temp.	1.0103	1.03	[1.0102-1.0105]	<.0001
	Daily Rain	1.0004	0.04	[1.0003-1.0005]	0.0042
	Wind Speed	1.0003	0.03	[0.9992-1.0013]	0.1597
	Daily Snow	1.0001	0.01	[0.9993-1.0009]	0.8279
	$PM_{2.5}$	1.0002	0.02	[1.0001-1.0003]	0.0089

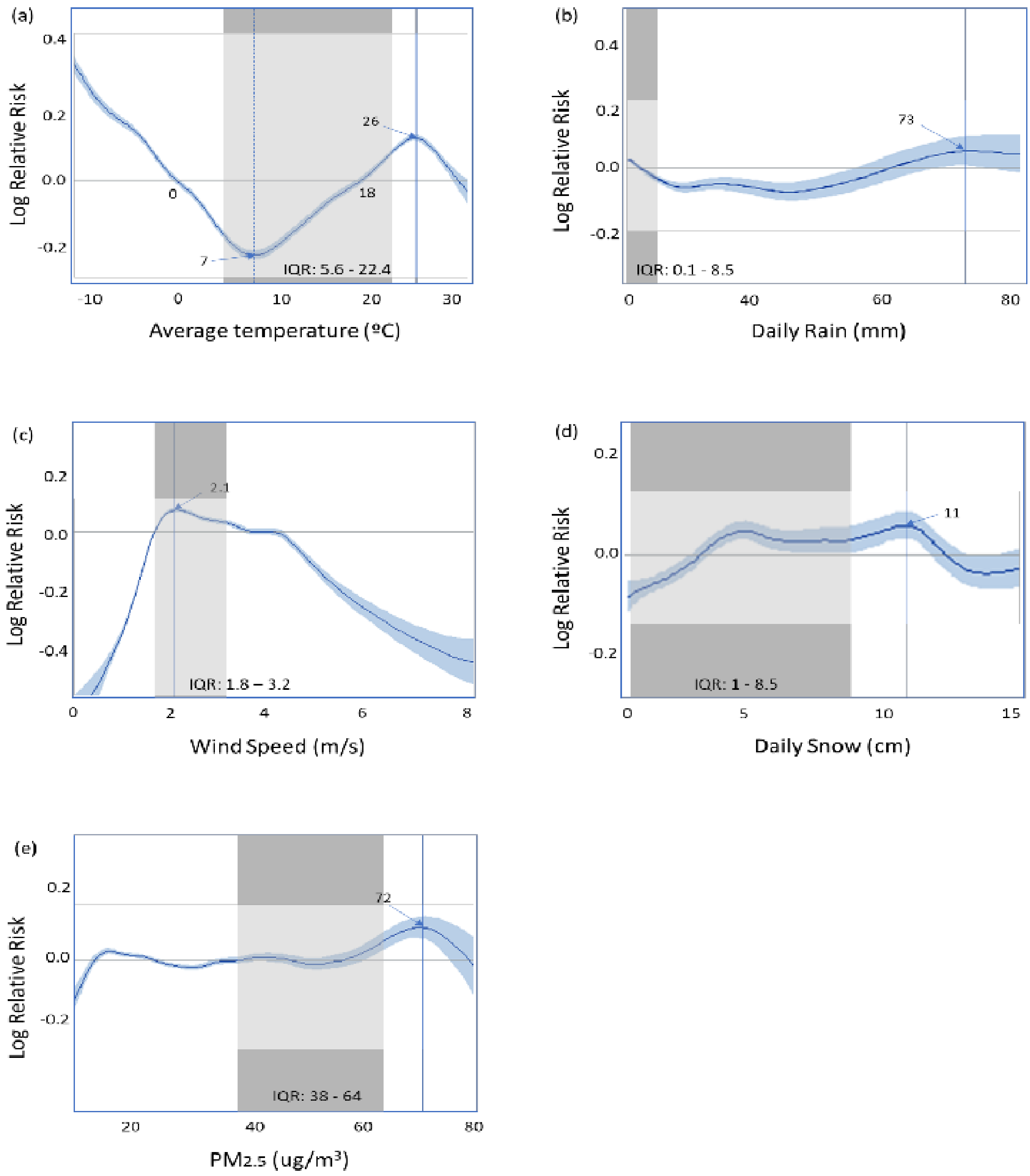
Supplemental Figure 1. Generalized additive model for the effects of selected meteorological factors on the incidence of knee fracture by: (a) average temperature, (b) daily rain, (c) wind speed, (d) daily snow, and (e) particulate matter ≤ 2.5 μm ($PM_{2.5}$). The bold line estimates the relative effect sizes for knee fracture, and the blue area estimates 95% confidence intervals (CIs).The X-axis represents selected meteorological factors. The Y-axes show the relative effect sizes for knee fracture. $PM_{2.5}$, particulate matter ≤ 2.5 μm.



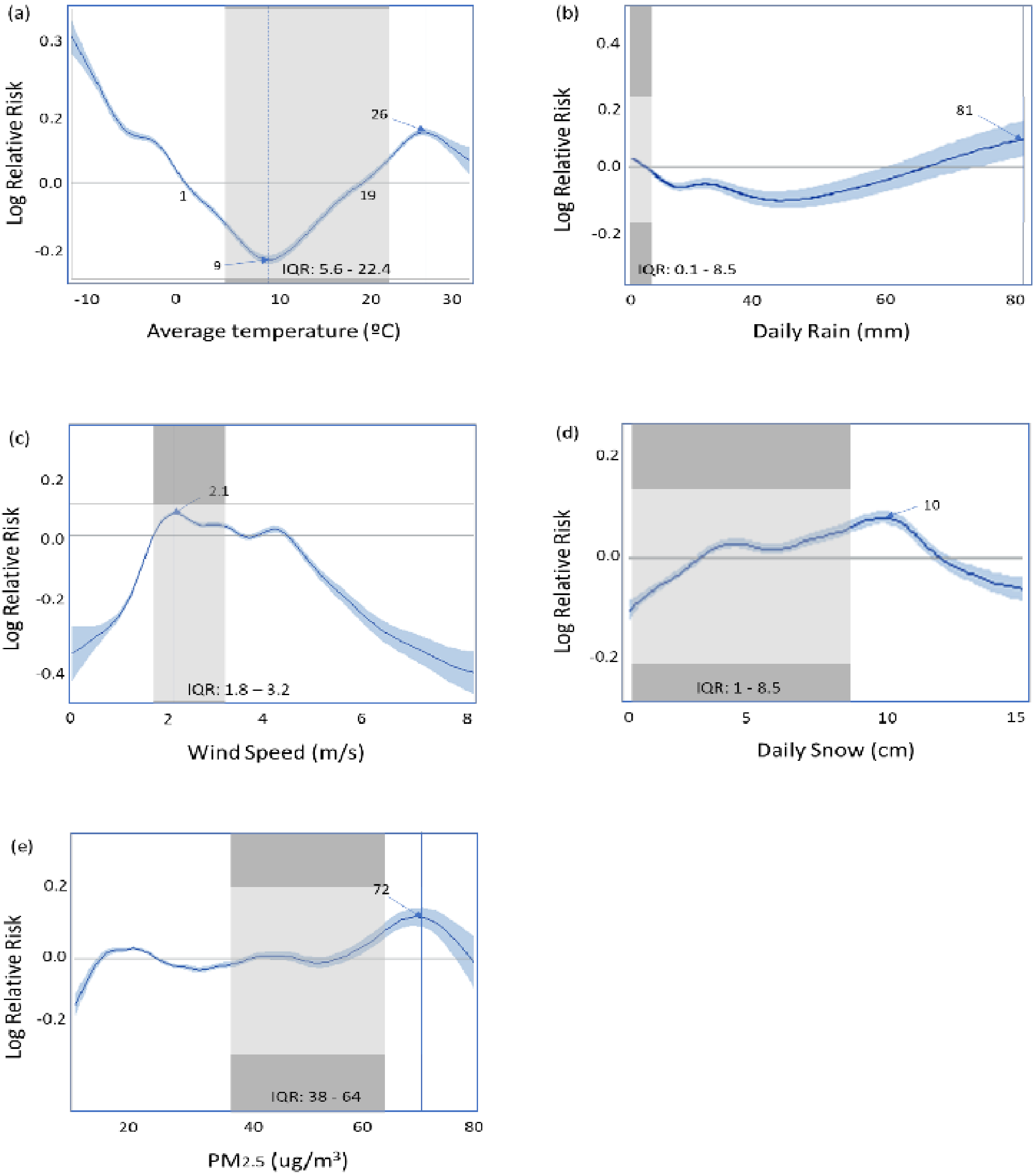
Supplemental Figure 2. Generalized additive model for the effects of selected meteorological factors on the incidence of shoulder fracture by: (a) average temperature, (b) daily rain, (c) wind speed, (d) daily snow, and (e) particulate matter ≤ 2.5 µm ($PM_{2.5}$). The bold line estimates the relative effect sizes for shoulder fracture, and the blue area estimates 95% confidence intervals (CIs). The X-axis represents selected meteorological factors. The Y-axes show the relative effect sizes for shoulder fracture. $PM_{2.5}$, particulate matter ≤ 2.5 µm.



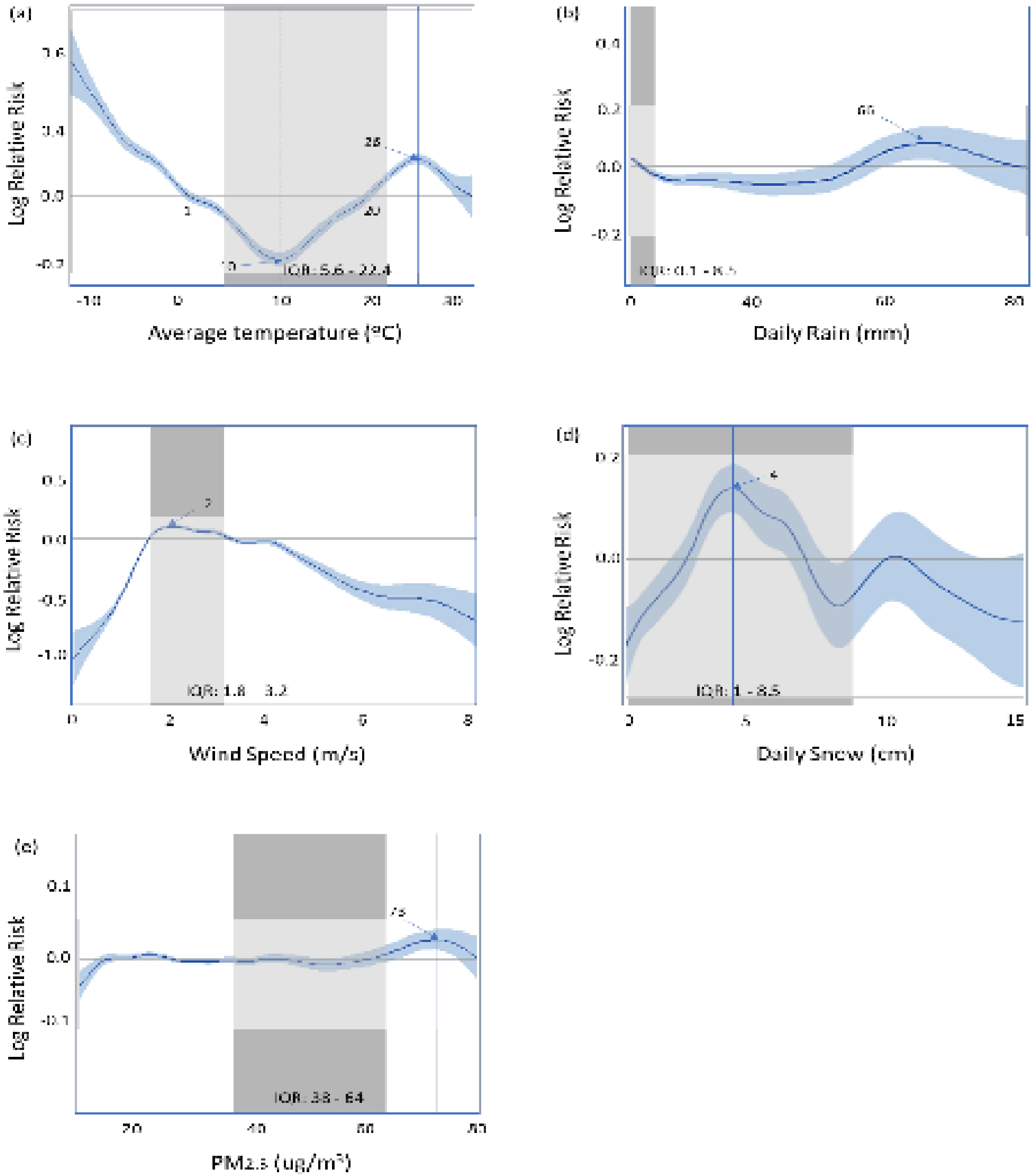
Supplemental Figure 3. Generalized additive model for the effects of selected meteorological factors on the incidence of elbow fracture by: (a) average temperature, (b) daily rain, (c) wind speed, (d) daily snow, and (e) particulate matter ≤ 2.5 μm ($PM_{2.5}$). The bold line estimates the relative effect sizes for elbow fracture, and the blue area estimates 95% confidence intervals (CIs). The X-axis represents selected meteorological factors. The Y-axes show the relative effect sizes for elbow fracture. $PM_{2.5}$, particulate matter ≤ 2.5 μm.



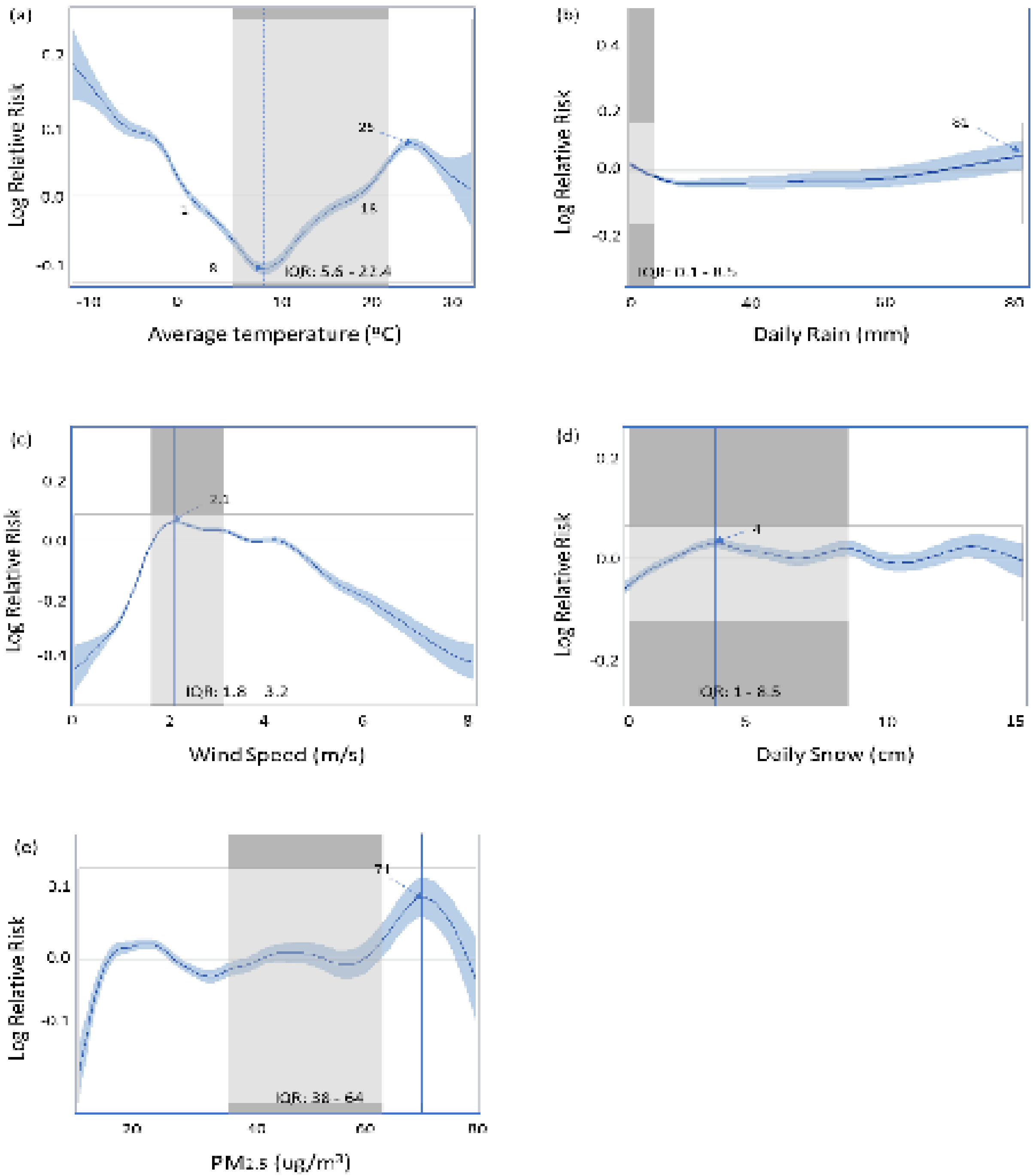
Supplemental Figure 4. Generalized additive model for the effects of selected meteorological factors on the incidence of wrist fracture by: (a) average temperature, (b) daily rain, (c) wind speed, (d) daily snow, and (e) particulate matter ≤ 2.5 μm ($PM_{2.5}$). The bold line estimates the relative effect sizes for wrist fracture, and the blue area estimates 95% confidence intervals (CIs). The X-axis represents selected meteorological factors. The Y-axes show the relative effect sizes for wrist fracture. $PM_{2.5}$, particulate matter ≤ 2.5 μm.



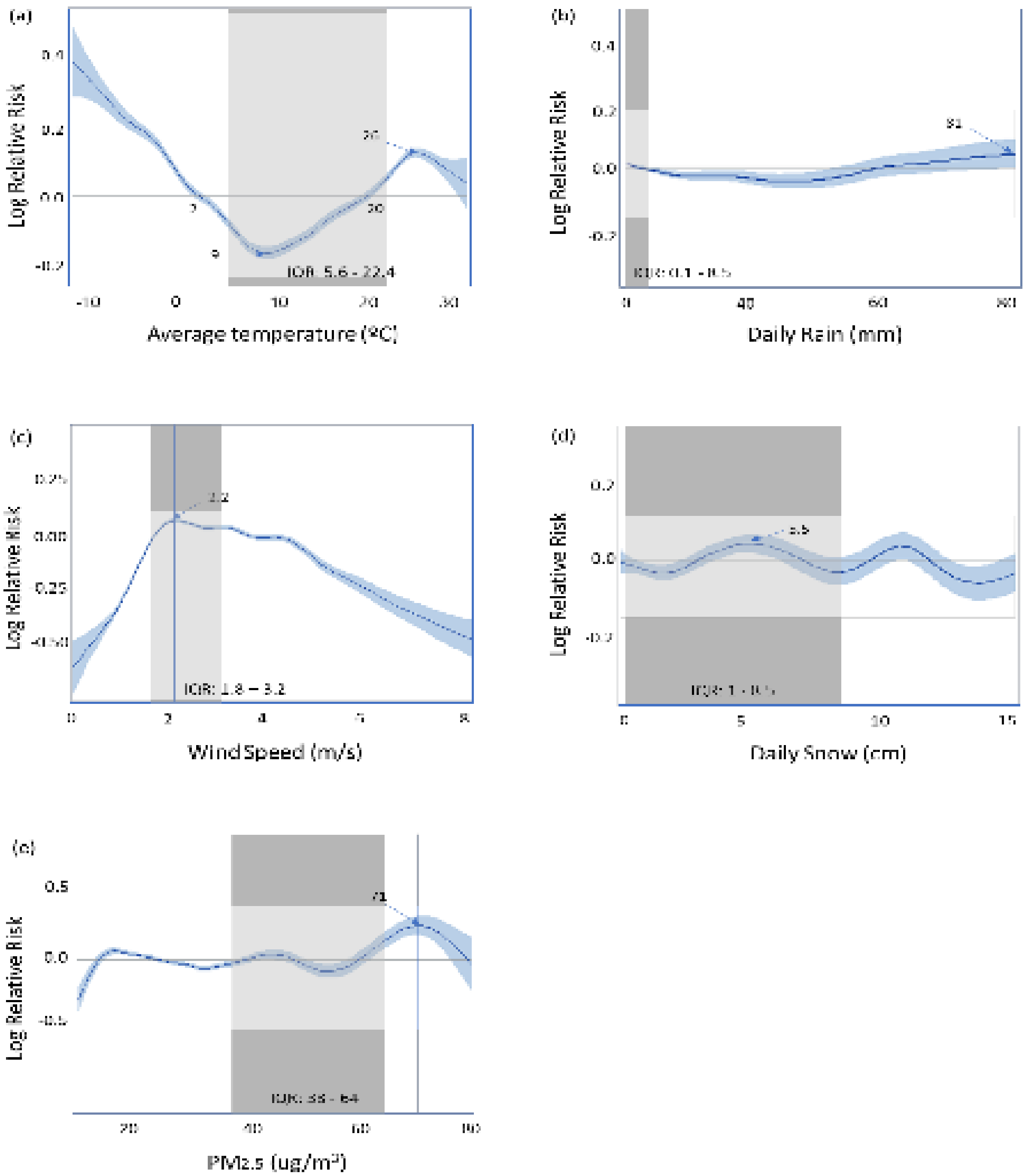
Supplemental Figure 5. Generalized additive model for the effects of selected meteorological factors on the incidence of hand fracture by: (a) average temperature, (b) daily rain, (c) wind speed, (d) daily snow, and (e) particulate matter ≤ 2.5 µm ($PM_{2.5}$). The bold line estimates the relative effect sizes for hand fracture, and the blue area estimates 95% confidence intervals (CIs). The X-axis represents selected meteorological factors. The Y-axes show the relative effect sizes for hand fracture. $PM_{2.5}$, particulate matter ≤ 2.5 µm.



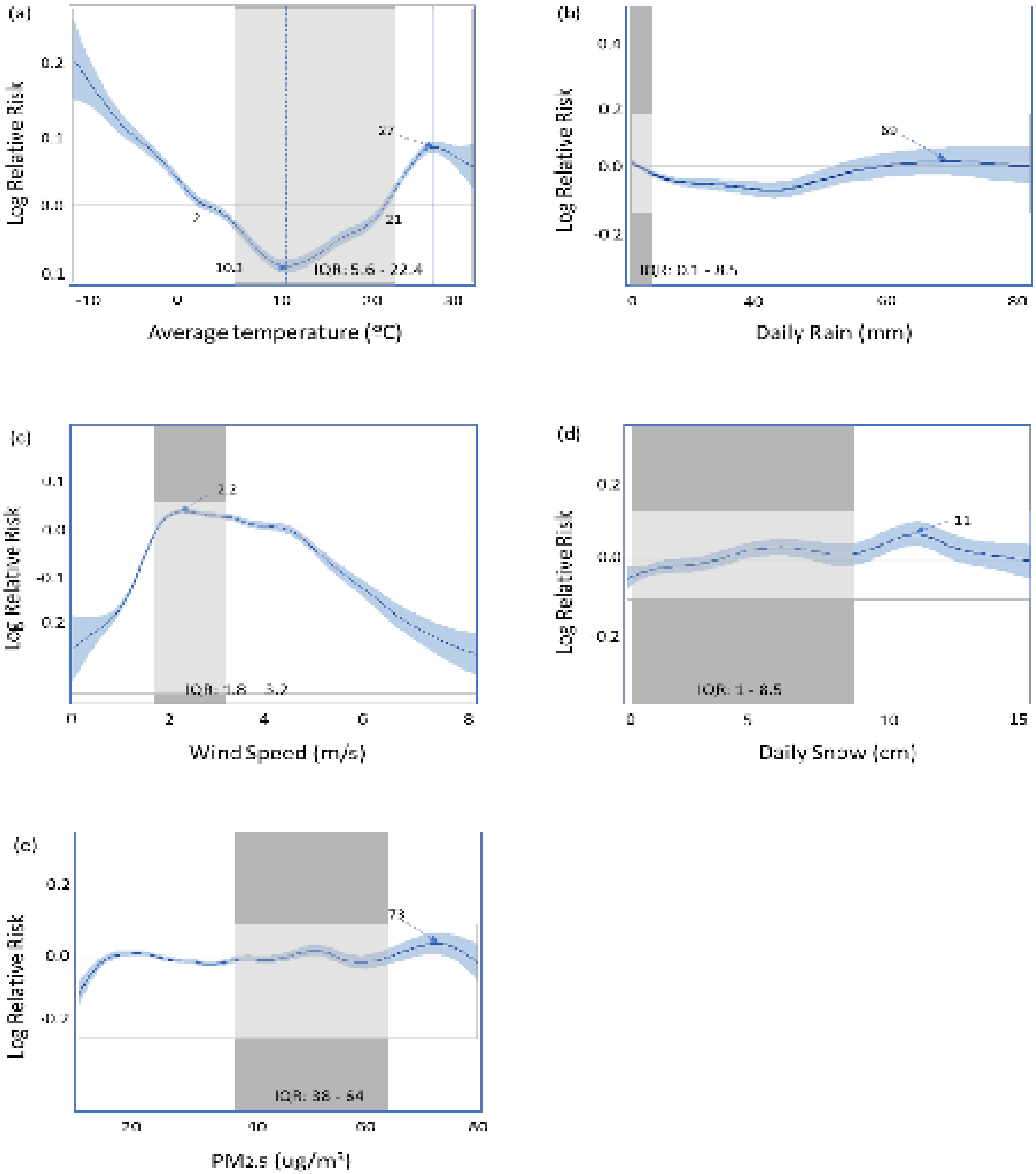
Supplemental Figure 6. Generalized additive model for the effects of selected meteorological factors on the incidence of ankle fracture by: (a) average temperature, (b) daily rain, (c) wind speed, (d) daily snow, and (e) particulate matter ≤ 2.5 μm ($PM_{2.5}$). The bold line estimates the relative effect sizes for ankle fracture, and the blue area estimates 95% confidence intervals (CIs). The X-axis represents selected meteorological factors. The Y-axes show the relative effect sizes for ankle fracture. $PM_{2.5}$, particulate matter ≤ 2.5 μm.



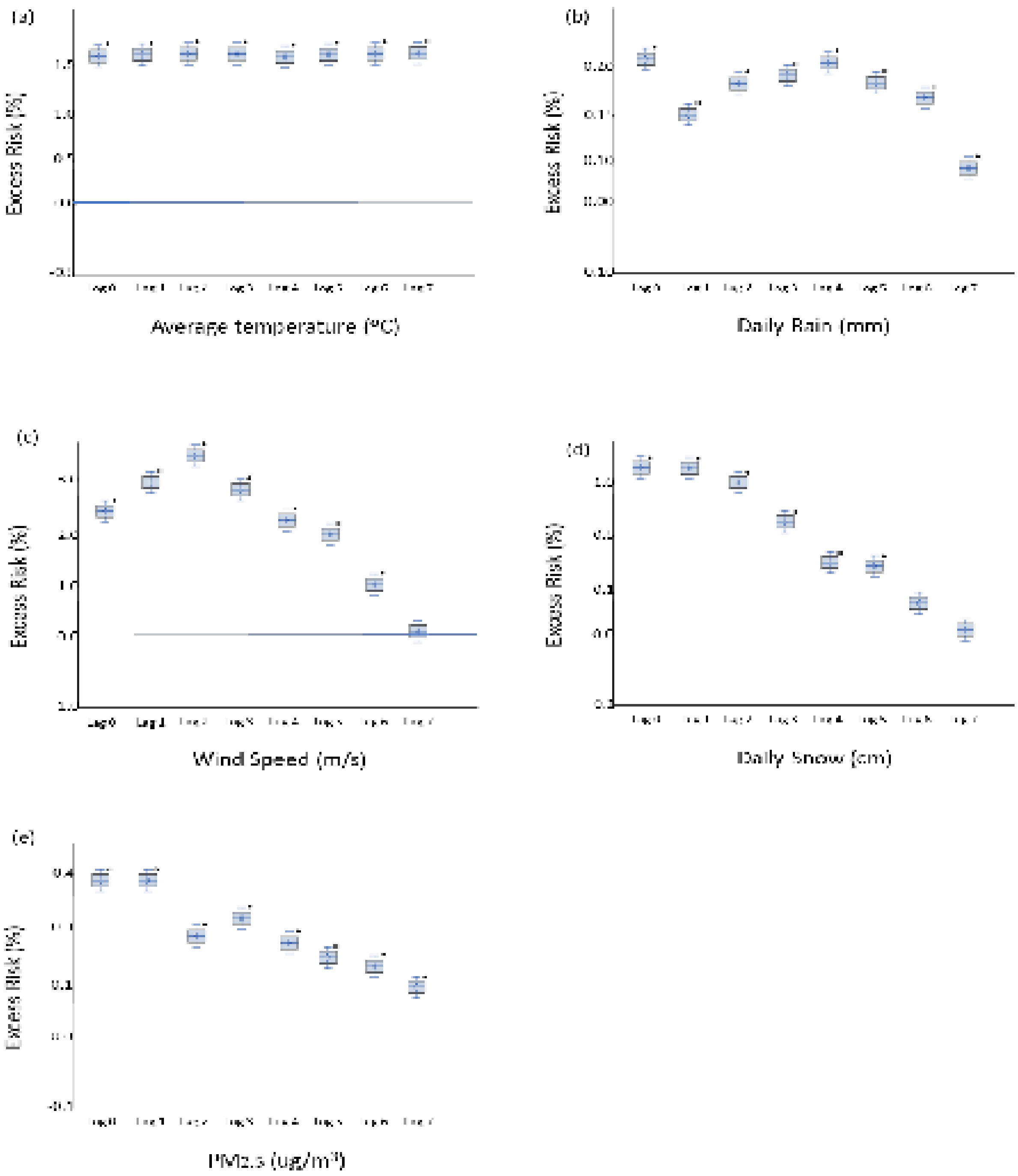
Supplemental Figure 7. Generalized additive model for the effects of selected meteorological factors on the incidence of foot fracture by: (a) average temperature, (b) daily rain, (c) wind speed, (d) daily snow, and (e) particulate matter ≤ 2.5 μm ($PM_{2.5}$). The bold line estimates the relative effect sizes for foot fracture, and the blue area estimates 95% confidence intervals (CIs). The X-axis represents selected meteorological factors. The Y-axes show the relative effect sizes for foot fracture. $PM_{2.5}$, particulate matter ≤ 2.5 μm.



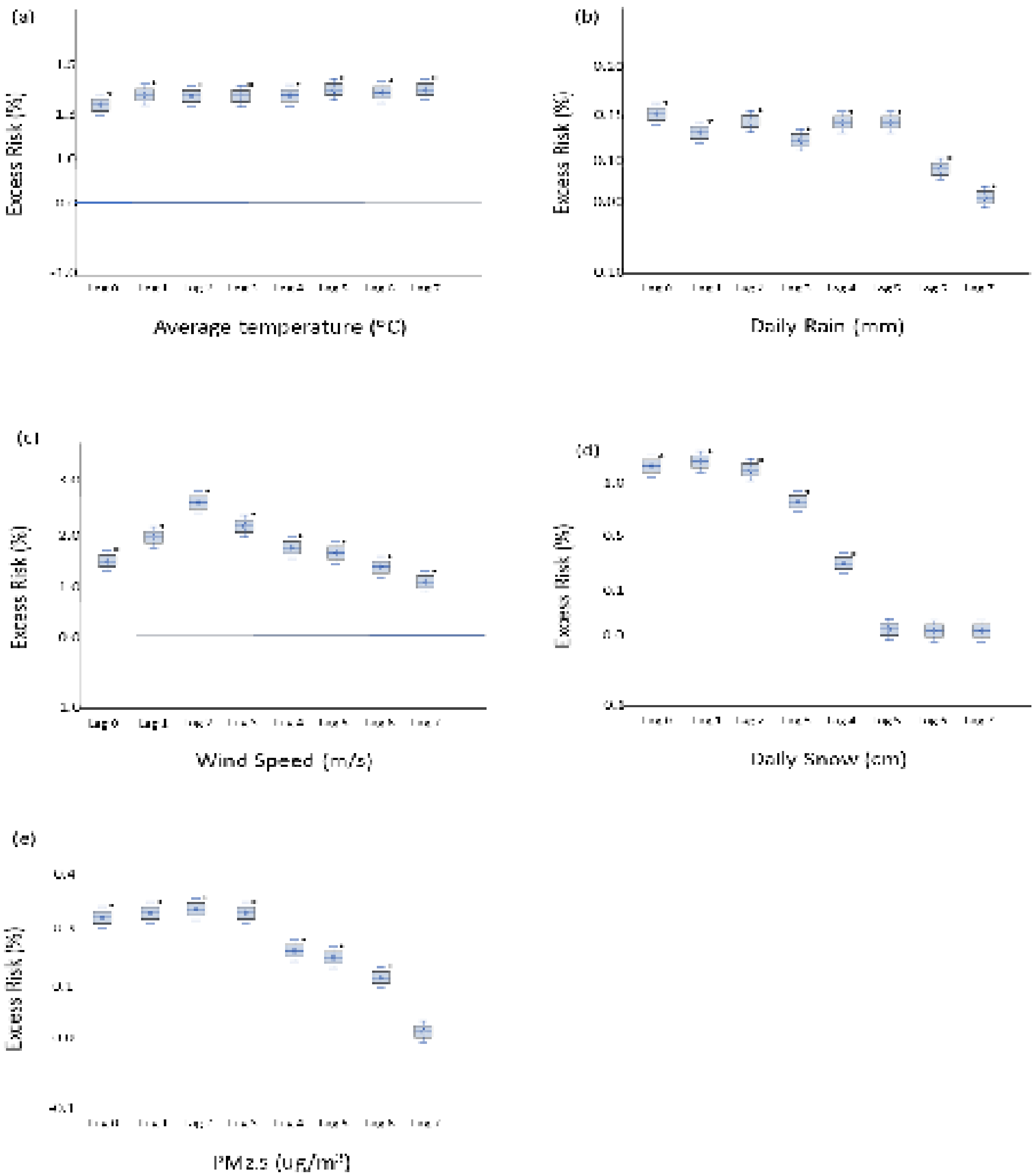
Supplemental Figure 8. Generalized additive model for the effects of selected meteorological factors on the incidence of spine fracture by: (a) average temperature, (b) daily rain, (c) wind speed, (d) daily snow, and (e) particulate matter ≤ 2.5 μm ($PM_{2.5}$). The bold line estimates the relative effect sizes for spine fracture, and the blue area estimates 95% confidence intervals (CIs). The X-axis represents selected meteorological factors. The Y-axes show the relative effect sizes for spine fracture. $PM_{2.5}$, particulate matter ≤ 2.5 μm.



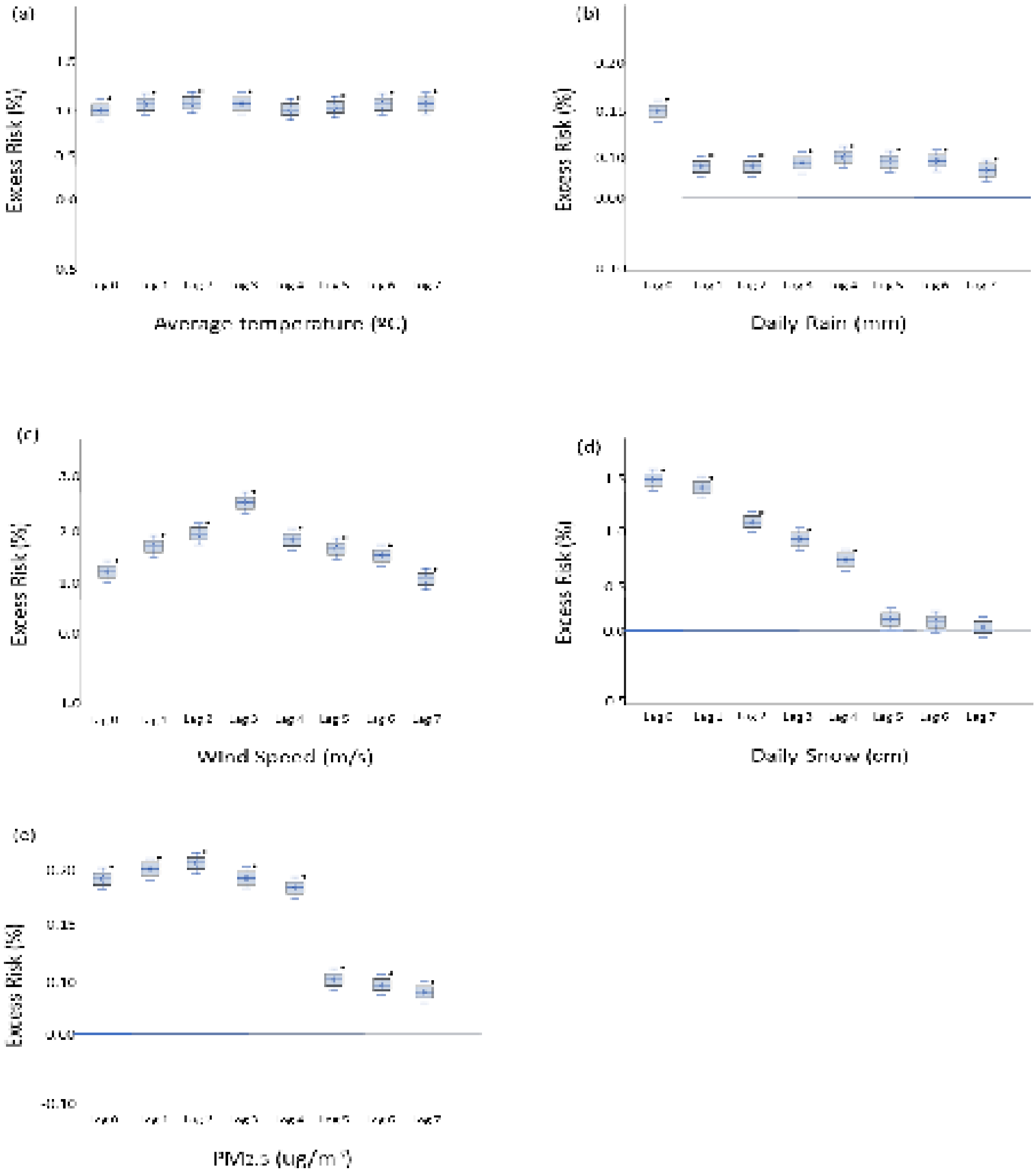
Supplemental Figure 9. Levels of the selected meteorological factors and adjusted excess risks of the knee fracture by: (a) average temperature, (b) daily rain, (c) wind speed, (d) daily snow, and (e) particulate matter ≤ 2.5 μm ($PM_{2.5}$). The Y-axes show the percentages of the adjusted excess risks with 95% confidence intervals (CIs). *P<.05.



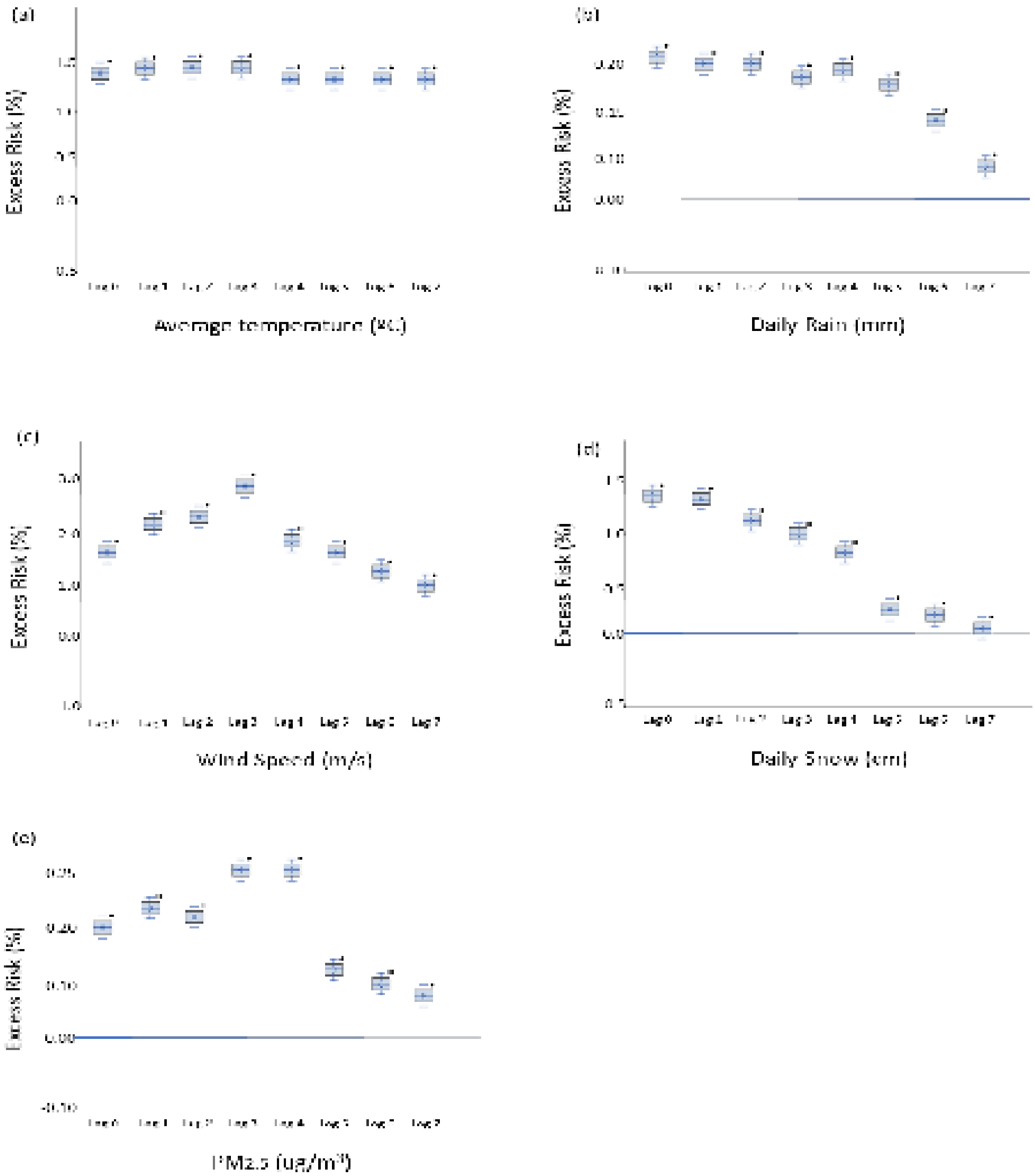
Supplemental Figure 10. Levels of the selected meteorological factors and adjusted excess risks of the shoulder fracture by: (a) average temperature, (b) daily rain, (c) wind speed, (d) daily snow, and (e) particulate matter ≤ 2.5 μm ($PM_{2.5}$). The Y-axes show the percentages of the adjusted excess risks with 95% confidence intervals (CIs). **P*<.05.



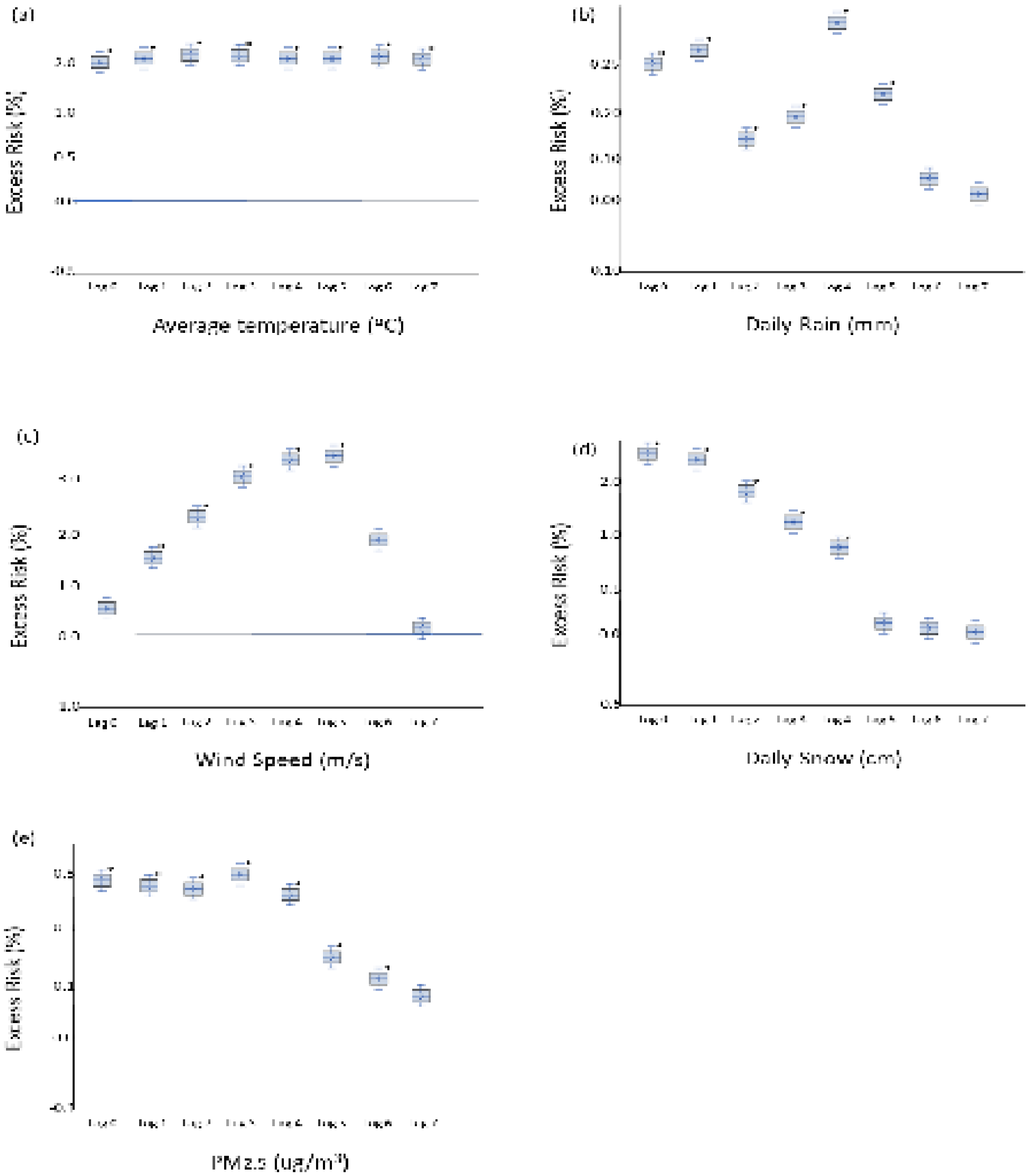
Supplemental Figure 11. Levels of the selected meteorological factors and adjusted excess risks of the elbow fracture by: (a) average temperature, (b) daily rain, (c) wind speed, (d) daily snow, and (e) particulate matter ≤ 2.5 μm ($PM_{2.5}$). The Y-axes show the percentages of the adjusted excess risks with 95% confidence intervals (CIs). *P<.05.



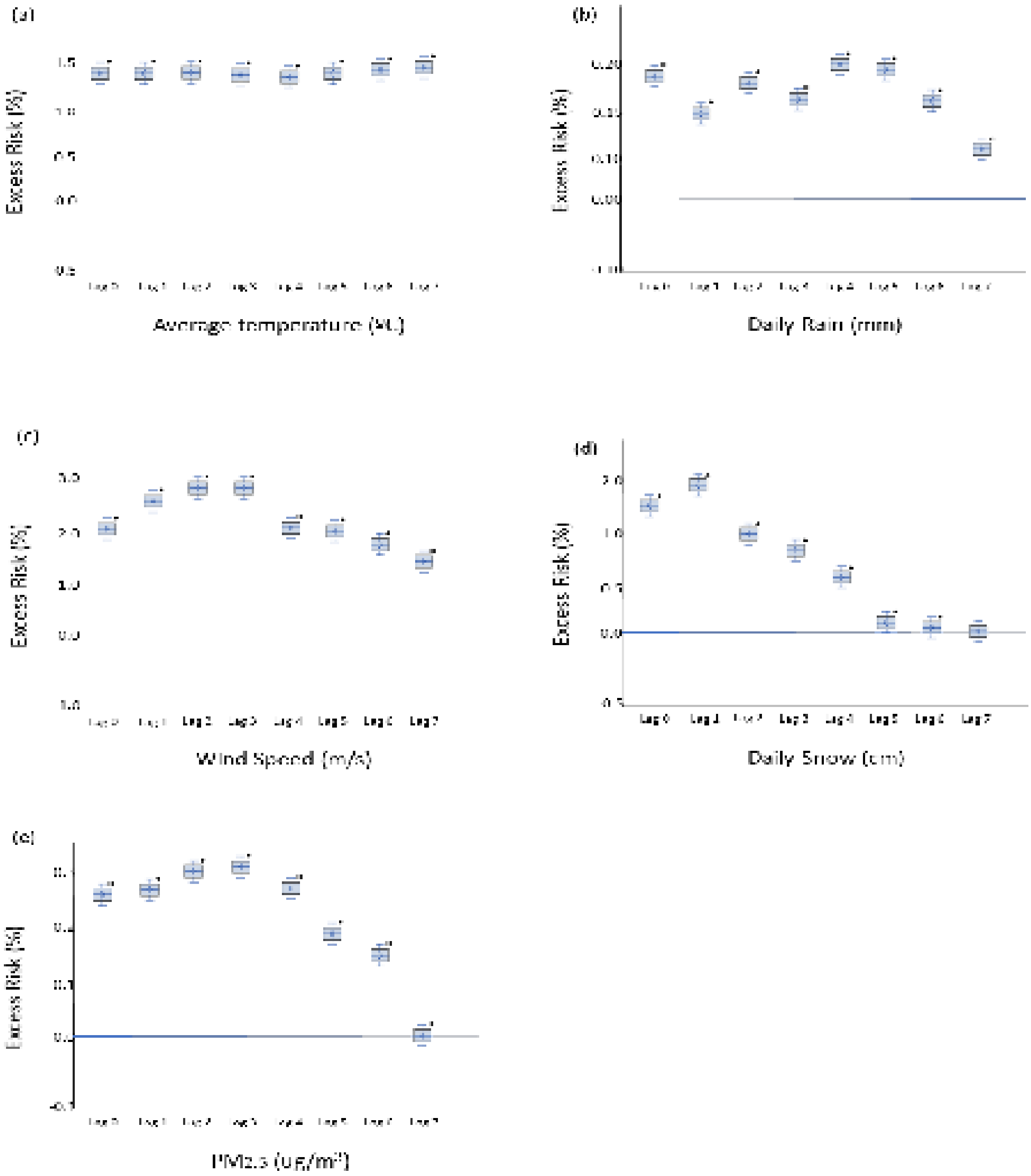
Supplemental Figure 12. Levels of the selected meteorological factors and adjusted excess risks of the wrist fracture by: (a) average temperature, (b) daily rain, (c) wind speed, (d) daily snow, and (e) particulate matter ≤ 2.5 μm ($PM_{2.5}$). The Y-axes show the percentages of the adjusted excess risks with 95% confidence intervals (CIs). **P*<.05.



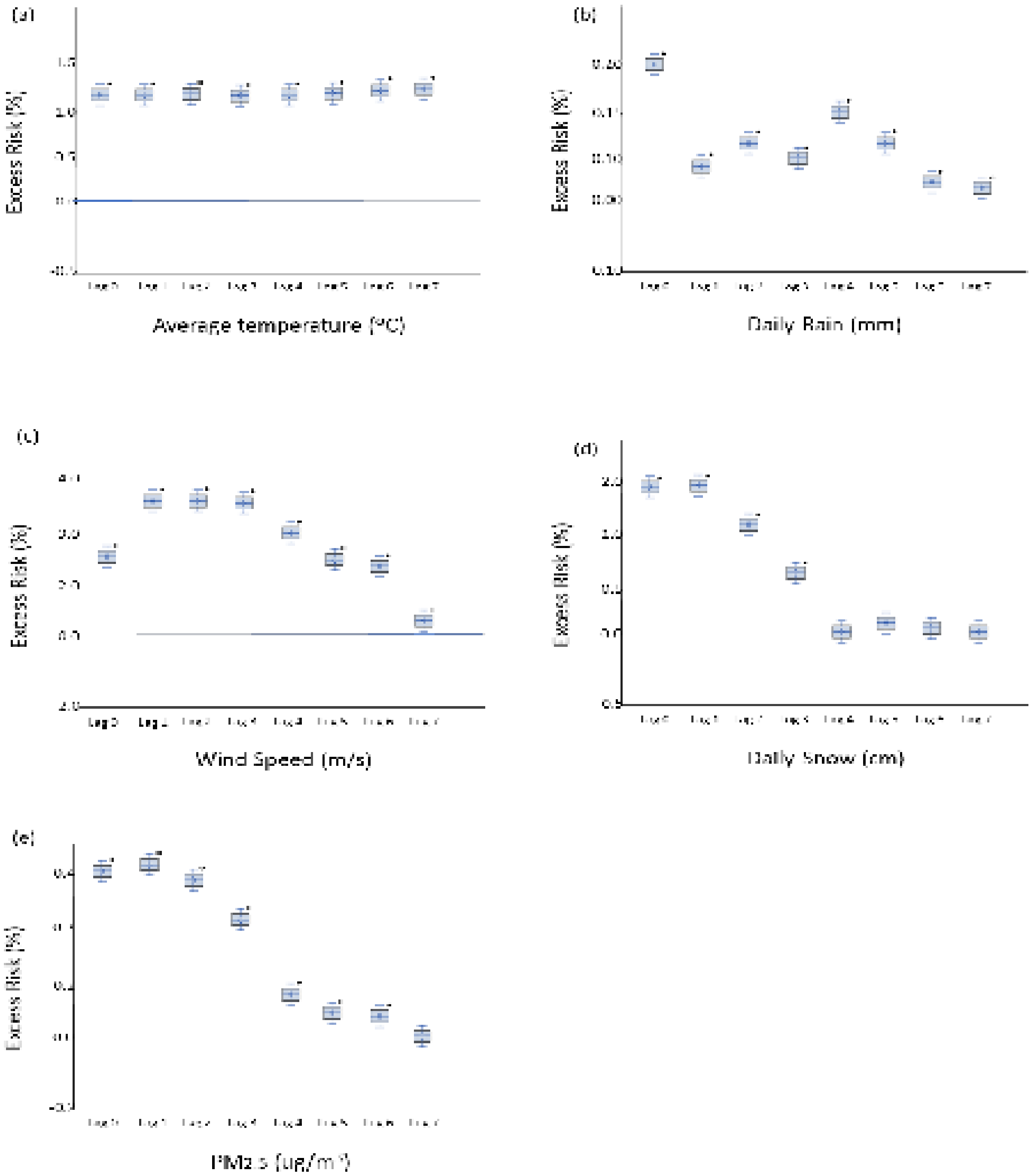
Supplemental Figure 13. Levels of the selected meteorological factors and adjusted excess risks of the hand fracture by: (a) average temperature, (b) daily rain, (c) wind speed, (d) daily snow, and (e) particulate matter ≤ 2.5 μm ($PM_{2.5}$). The Y-axes show the percentages of the adjusted excess risks with 95% confidence intervals (CIs). **P*<.05.



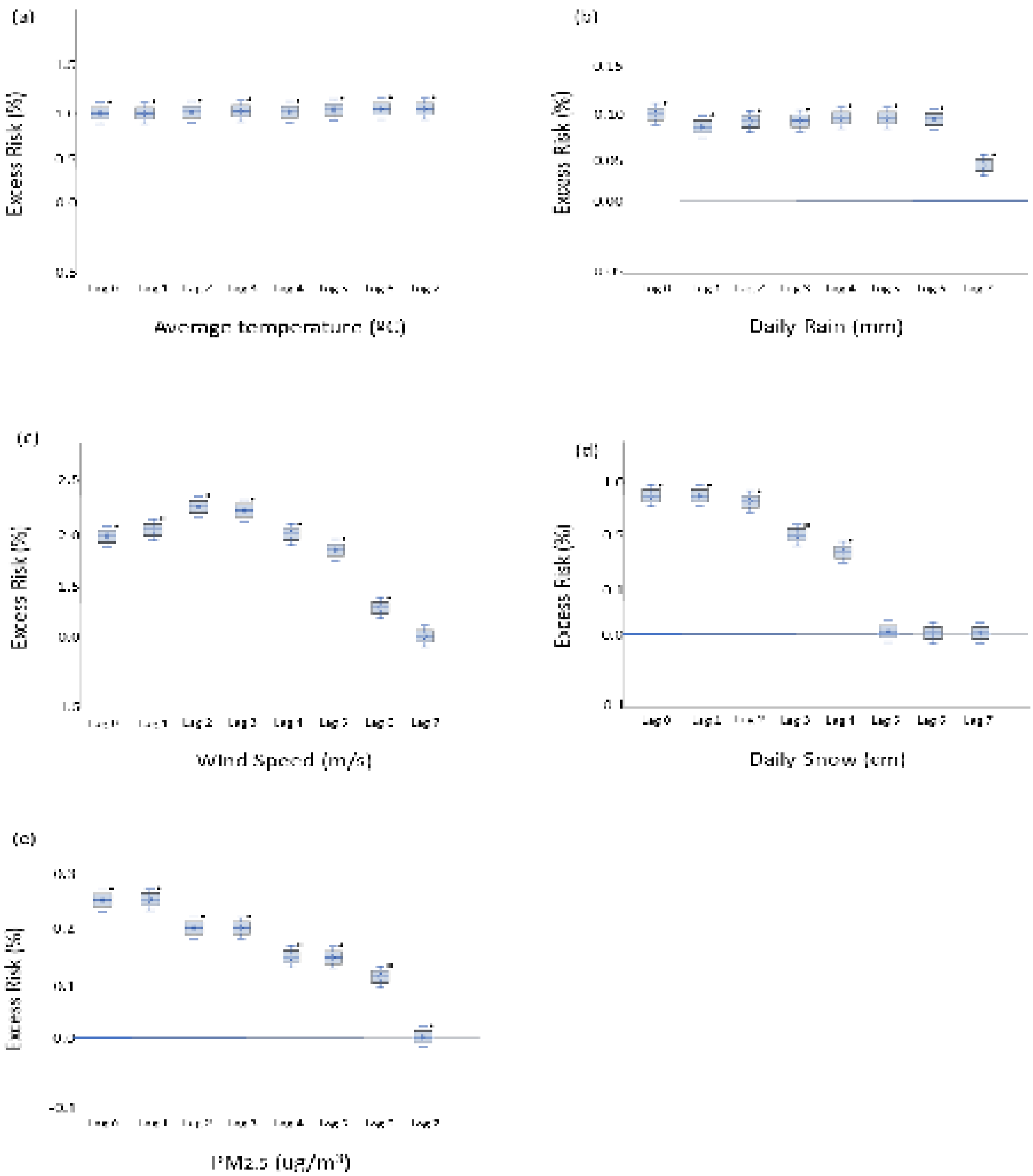
Supplemental Figure 14. Levels of the selected meteorological factors and adjusted excess risks of the ankle fracture by: (a) average temperature, (b) daily rain, (c) wind speed, (d) daily snow, and (e) particulate matter ≤ 2.5 μm ($PM_{2.5}$). The Y-axes show the percentages of the adjusted excess risks with 95% confidence intervals (CIs). **P*<.05.



Supplemental Figure 15. Levels of the selected meteorological factors and adjusted excess risks of the foot fracture by: (a) average temperature, (b) daily rain, (c) wind speed, (d) daily snow, and (e) particulate matter ≤ 2.5 μm ($PM_{2.5}$). The Y-axes show the percentages of the adjusted excess risks with 95% confidence intervals (CIs). **P*<.05.



Supplemental Figure 16. Levels of the selected meteorological factors and adjusted excess risks of the spine fracture by: (a) average temperature, (b) daily rain, (c) wind speed, (d) daily snow, and (e) particulate matter ≤ 2.5 μm ($PM_{2.5}$). The Y-axes show the percentages of the adjusted excess risks with 95% confidence intervals (CIs). **P*<.05.



STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1,3,4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (*b*) For matched studies, give matching criteria and number of exposed and unexposed	7 fig1
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7,8
Bias	9	Describe any efforts to address potential sources of bias	14
Study size	10	Explain how the study size was arrived at	fig1
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding (*b*) Describe any methods used to examine subgroups and interactions (*c*) Explain how missing data were addressed (*d*) If applicable, explain how loss to follow-up was addressed (*e*) Describe any sensitivity analyses	8,9
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	9 fig1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	9, fig2, Sup Tab1
Outcome data	15*	Report numbers of outcome events or summary measures over time	9, fig2

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	9,10
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.