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Mortality Risk of Hot Nights: A Nationwide Population-Based Retrospective Study in Japan

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Background: The health effects of heat are well documented; however, limited information is available regarding the health risks of hot nights. Hot nights have become more common, increasing at a faster rate than hot days, making it urgent to understand the characteristics of the hot night risk.

Objectives: We estimated the effects of hot nights on the cause- and location-specific mortality in a nationwide assessment over 43 y (1973–2015) using a unified analytical framework in the 47 prefectures of Japan.

Methods: Hot nights were defined as days with *a*) minimum temperature ≥25°C (HN_{25}) and *b*) minimum temperature ≥95th percentile (HN_{95th}) for the prefecture. We conducted a time-series analysis using a two-stage approach during the hot night occurrence season (April–November). For each prefecture, we estimated associations between hot nights and mortality controlling for potential confounders including daily mean temperature. We then used a random-effects meta-analytic model to estimate the pooled cumulative association.

Results: Overall, 24,721,226 deaths were included in this study. Nationally, all-cause mortality increased by 9%–10% [HN_{25} relative risk (RR) = 1.09, 95% confidence interval (CI): 1.08, 1.10; HN_{95th} RR = 1.10, 95% CI: 1.09, 1.11] during hot nights in comparison with nonhot nights. All 11 cause-specific mortalities were strongly associated with hot nights, and the corresponding associations appeared to be acute and lasted a few weeks, depending on the cause of death. The strength of the association between hot nights and mortality varied among prefectures. We found a higher mortality risk from hot nights in early summer in comparison with the late summer in all regions.

Conclusions: Our findings support the evidence of mortality impacts from hot nights in excess of that explicable by daily mean temperature and have implications useful for establishing public health policy and research efforts estimating the health effects of climate change. https://doi.org/10.1289/EHP11444

Introduction

Due to progressing global warming, the frequency and intensity of extreme heat events have increased, and hot days and nights are expected to be more frequent in the near future.[1,2] Exposure to excessive heat has broad physiological impacts on humans, often intensifying preexisting health conditions and resulting in premature deaths.[3] The effects of several heat characteristics on mortality have been well documented in epidemiological studies; however, many investigators generally considered daytime heat using the daily maximum temperature[4] or overall heat using the daily mean temperature index.[5,6] However, the daily minimum temperature plays a significant role in health because if the overnight temperature does not fall below a certain threshold value (T_{thresh}), people are unable to cool down and recover from the daytime heat, meaning that they are more likely to develop heat-related health problems.[7] Accordingly, hot nights could impose an extra burden on the body because nighttime offers natural heat relief, suggesting that the daily minimum temperature can be considered a risk factor for heat-induced illness. Moreover, hot nights are becoming increasingly important in health studies because daily minimum temperatures are rising quicker than daily maximum temperatures and will continue to do so in the future.[1,8]

To date, few studies have investigated the association between hot night–related mortality risks and were conducted in a single city in Europe[9,10] or in several cities in southern Europe.[11] Because the associations between heat and health vary substantially by location, the results are not conclusive regarding the existence and size of hot night effects on mortality in different regions.

Japan, an island nation, is severely affected by climate change as are other countries around the world. Japan's annual mean surface temperature increased by 1.19°C over the past 100 y, whereas global temperature has increased by 0.72°C in that same period.[12] In addition, the former is expected to rise another 0.5–5.4°C, which is higher than the global average of 0.3° to 4.8°C, depending on the representative concentration pathway scenario over the next century, indicating that the Japanese population is at increased risk for climate-related health effects in the near future.[12,13]

In this study, we used a national data set to investigate the association between hot nights and the risk of mortality from 1973 to 2015 in Japan. Hot nights were defined using physiology- and community-based T_{thresh} to explore the possibilities of adaptation to the local climate. Our investigation focused on three aspects of the hot night–mortality association as follows: *a*) All-cause and 11 cause-specific analyses were performed, and their lag structures were investigated to understand the possible mechanism causing hot night–related mortality; *b*) We explored the geographical variation in these associations across prefectures to identify areas with both frequent hot nights and particularly vulnerable subpopulations, which was facilitated by significant differences in climate

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between the north and south (though Japan has a relatively small area and fairly uniform demography and culture), and we performed a meta-regression to better elucidate the between-prefecture heterogeneity of the mortality risk associated with hot nights; and *c*) An assessment of intraseason variability in the risk was conducted as changes in the susceptibility of a population to hot nights during the summer may be associated with acclimatization and other adaptive behaviors. To the best of our knowledge, this study is the first investigation to examine the association between hot nights and mortality nationwide.

Methods

Study Area

The Japanese archipelago consists of 6,852 mountainous islands located on the northeastern end of Asia (Figure 1; Excel Table S1). The main four islands are Hokkaido, Honshu, Shikoku, and Kyushu, and Japan is divided into 47 prefectures in 8 regions, with Hokkaido (P1; R1; latitude from 41°N to 45°N) being the northernmost prefecture and Okinawa (P47; R8; 24°N to 28°N) being the southernmost prefecture (Figure S1). The climate in Japan is mostly temperate, with four distinct seasons. However, because of the wide latitude range of Japan, northern Japanese regions, including the Hokkaido and Honshu highlands, have a subarctic climate, whereas the southern parts have a subtropical climate.[14] Moreover, there is noticeable climate variability between Japanese seaside and inland regions (Figure S2); distributions of the daily mean temperature differ among prefectures after accounting for a comparatively small area (Figure S3).

Data

Analysis was based on prefecture-specific daily weather conditions and mortality counts in Japan, which include the entire population between 1973 and 2015. Meteorological data were provided by the Japan Meteorological Agency (JMA)[15] for the aforementioned period (Table S2). In Japan, hot nights, also called tropical nights, or *Nettaiya* in Japanese, are officially defined by the JMA as days on which the daily minimum temperature exceeds 25°C (HN_{25}). Because HN_{25} occurred only between April and November during the study period, analyses were restricted to these months (Figure S4; Excel Table S2). In addition to this fixed absolute T_{thresh} (physiology-based), community-based T_{thresh} was used to define a hot night as days on which the daily minimum temperature exceeded the 95th percentile of the daily minimum temperatures of that prefecture during the study period (HN_{95th}). The proportion of missing temperature data during the study period ranged from 0% to 0.095% across the 47 prefectures. Given the low rate of missing data, we chose not to impute the missing temperature data to avoid potential errors. Daily mortality data were obtained from the Ministry of Health, Labor, and Welfare of Japan (Table S1). In line with the *International Classification of Diseases* (ICD) codes, deaths were classified by 11 specific causes: cardiovascular diseases (CVD), ischemic heart disease (IHD), cerebrovascular disease (CBVD), cerebral hemorrhage (CH), cerebral infarction (CIN), respiratory disease (RD), pneumonia, chronic obstructive pulmonary disease (COPD), asthma, renal disease, and advanced age. Corresponding ICD codes can be found in Table S3. Moreover, age-stratified all-cause mortality was grouped as <15, 15–65, and ≥65 y old (Figure S5). The nature of the data collected as daily counts meant that no identifiable information was included; therefore, the research was exempt from institutional review board approval.

Statistical Analyses

The association between hot nights and mortality was examined with a two-stage hierarchal approach using data from 47 prefectures

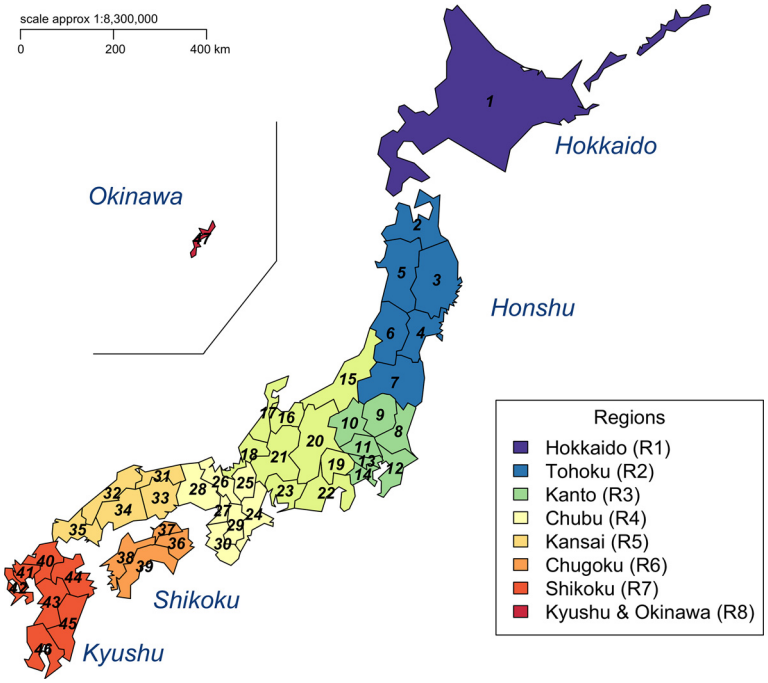

Figure 1. Study locations including 47 prefectures in 8 Japanese regions. The main four islands are Hokkaido, Honshu, Shikoku, and Kyushu (see Excel Table S1 for prefecture numbers and region definitions). 1. Hokkaido, 2. Aomori, 3. Iwate, 4. Miyagi, 5. Akita, 6. Yamagata, 7. Fukushima, 8. Ibaraki, 9. Tochigi, 10. Gunma, 11. Saitama, 12. Chiba, 13. Tokyo, 14. Kanagawa, 15. Niigata, 16. Toyama, 17. Ishikawa, 18. Fukui, 19. Yamanashi, 20. Nagano, 21. Gifu, 22. Shizuoka, 23. Aichi, 24. Mie, 25. Shiga, 26. Kyoto, 27. Osaka, 28. Hyogo, 29. Nara, 30. Wakayama, 31. Tottori, 32. Shimane, 33. Okayama, 34. Hiroshima, 35. Yamaguchi, 36. Tokushima, 37. Kagawa, 38. Ehime, 39. Kochi, 40. Fukuoka, 41. Saga, 42. Nagasaki, 43. Kumamoto, 44. Oita, 45. Miyazaki, 46. Kagoshima, and 47. Okinawa.

in 8 regions. A time-series quasi-Poisson regression model for seasonal data based on a generalized linear model was applied to derive the estimates of hot nights on prefecture-specific mortality, reported as relative risk (RR). The mortality risk for hot nights was compared with nonhot nights, controlling for the daily mean temperature to separate the overall heat effects from those of hot nights, referring to the added hot night effect. By considering an indicator variable for hot nights, we avoided significant correlations with the daily mean temperatures, and this approach is similar to methods used in previous heatwave studies to compare mortality risk on heatwave days with non–heat wave days.[5,16]

The association with hot nights was specified with a distributed lag model (DLM), with a natural cubic spline with 3 degrees of freedom (df) for 21 d by applying three internal knots at equal intervals in the log scale for a lag–response curve.[17] Daily mean temperature was included in the model as a cross-basis (CB) function adopting a distributed lag nonlinear model (DLNM). Specifically, an exposure–response curve was modeled by a natural cubic spline with 3 df and two internal knots and a lag–response curve with three internal knots at equal intervals in the log scale with the same lag period as hot nights (21 d). We considered multiple time series in DLM for hot nights and DLNM for temperature by breaking the series at the end of each year and replacing the first rows up to the maximum lag of the CB matrix in the following series with missing values (https://cran.r-project.org/web/packages/dlnm/vignettes/dlnmTS.pdf). Seasonality was controlled for by applying a natural cubic spline for the day of the year with 5 df. An interaction between a spline function and calendar year indicator was specified to relax the assumption of a constant seasonal trend. The model also included a natural cubic spline of time, with equally spaced knots and ~ 1 df every 10 y to control for long-term trends, and an indicator for the day of the week. The high dimensional effect estimates obtained from the distributed lag function were reduced to represent the hot night–mortality association accumulated over the lag days for each prefecture, and they were pooled into regional and national levels by performing meta-analyses based on a random-effect model in the second modeling stage.[18]

The between-prefecture heterogeneity of HN_{25} effects was further explored through the univariate meta-regression analyses, separately carried out for multiple variables as meta-predictors. We chose the air conditioning (AC) prevalence (percentage) defined as the proportion of households with two or more occupants with AC,[19] because it has been demonstrated to modify the risk of heat-related mortality.[20,21] Location information (latitude and longitude[22]) and the climate summary [mean, minimum, and maximum temperature (°C)[15]] were also included in the meta-analyses because it has previously been observed that the relation between heat and mortality vary with geographical location and the susceptibility differences were modified by the local climate.[23,24] In addition, sociodemographic characteristics have been found to modify the susceptibility to heat impacts; thus, demographic and socioeconomic characteristics were also included as meta-predictors in the meta-analyses.[25,26] The demographic predictors included the proportion of the elderly (percentage, proportion of the population age 65 y and older), and the female population (percentage, proportion of the female).[27] The socioeconomic predictors included the number of outpatients (average number of patients per day in general hospitals, expressed as a rate per 100,000 population),[28] Economic Power Index (EPI) (consecutive 3-y average of the ratio obtained by dividing the fiscal revenue by the fiscal demand, a higher value represents more financial strength of a local government[29]), and urbanization (densely inhabited districts by prefecture population, characterized by a population density of 4,000 or more people per square kilometer and a total population of 5,000 or more).[30] Detailed information for each data was provided in Excel Table S3. Residual heterogeneity was tested and then reported by the Cochran Q test and I^2 statistic.[31]

We examined the variation in all-cause mortality risk associated with hot nights during the season (April–November) by extending our DLM to a time-varying DLM, which was specified through an interaction between the CB of hot nights and time variables.[32] By centering on the days corresponding to the midpoint of June and August in the series, hot nights–mortality relationships for early and late summer were predicted. All data management and statistical analyses were performed using SAS (version 9.4; SAS Institute, Inc.) and R (version 4.1.1; R Development Core Team). Statistical significance was set at $p < 0.05$.

Sensitivity Analyses

Sensitivity analyses were performed to examine the strength of our findings. Relative humidity (RH) was tested as a possible confounder or effect modifier. RH was included in a model and compared with that of hot night estimates from our main model because a high humidity level is known to exacerbate the effects of heat stress by impairing the body's ability to sweat and cool itself.[33] We tested alternative maximum lag periods of 14 and 28 d in CB functions of hot nights and mean temperature (Table S4). Besides adjusting for mean temperature as a proxy of overall heat, supplementary analyses were conducted adjusting for daily maximum temperature, which is the single common summary of daytime heat in epidemiological studies (Figure S6; Excel Table S4). Furthermore, we estimated the added effects of hot nights on mortality related to heatwaves, which are defined as periods that have the 95th percentile of the daily mean temperature and last ≥ 2 d, by adding a heatwave variable as an additional adjustment in the model (Figure S7; Excel Table S5).

Results

Descriptive Statistics

During the study period, we observed 24,721,226 all-cause deaths, 8,094,644 cardiovascular-related deaths, and 3,015,164 respiratory-related deaths. Table S1 provides prefecture-specific statistics for the population in 2015 and mortality during the corresponding period. Daily mean temperature distribution in the northernmost prefecture, Hokkaido (P1; R1), showed two peaks with a wide range of daily mean temperatures (mean = 8.9°C, min = −14.1°C, max = 30.1°C), whereas that in the southernmost prefecture, Okinawa (P47; R8), showed a left-skewed distribution with a narrow range of daily mean temperatures (mean = 22.9°C, min = 9.1°C, max = 31.1°C) (Table S2; Figure S3). Extreme temperatures reached from a daily minimum of −19.4°C in Hokkaido (P1; R1) to a daily maximum of 40.9°C in Saitama (P11; R3) during the study period (Table S2). Hot nights defined with physiology-based T_{thresh} (HN_{25}) rarely occurred in northern regions, such as Hokkaido (P1; R1; 0.05 d/y), Iwate (P3; R2; 0.09 d/y), Aomori (P2; R2; 0.26 d/y), and Yamagata (P6; R2; 0.44 d/y). On the other hand, HN_{25}s were abundant in southern regions, such as Okinawa (P47; R8; 96 d/y), Kagoshima (P46; R8; 44.4 d/y), and Nagasaki (P42; R8; 33.47 d/y), as well as in populous metropolitan prefectures, such as Tokyo (P13; R3; 27.12 d/y) and Osaka (P27; R5; 35.77 d/y) (Table S2). Community-based T_{thresh} used to define HN_{95th} in each prefecture ranged from 20.64°C in Hokkaido (P1; R1) to 27.70°C in Okinawa (P47; R8), whereas it was around ~ 25°C in most of the regions of Chubu (R4), Kansai (R5), Chugoku (R6), and Shikoku (R7) (Table S2). Most prefectures experienced hot nights in July and August the most, and early or late hot

nights (i.e., in April or November) were rare (Figure S4; Excel Table S2).

Variation across Cause-Specific Subgroups and Their Lag Structures

The first set of analyses examined the impact of hot nights on cause-specific mortality and their lag structures. A substantially increased risk of cause-specific mortality was observed in all 11 causes of death on hot nights, and it is apparent that the cause-specific RRs and their lag structures of HN_{25} are similar to those of HN_{95th}. The association between hot nights and total CVD-related mortality (HN_{25} RR = 1.17, 95% CI: 1.15, 1.19; HN_{95th} RR = 1.17, 95% CI: 1.15, 1.19) was stronger than that between hot nights and all-cause mortality (HN_{25} RR = 1.09, 95% CI: 1.08, 1.10; HN_{95th} RR = 1.10, 95% CI: 1.09, 1.11). The CVD subdivisions, including IHD, CBVD, and CIN, showed higher risks than all-cause mortality, except CH (HN_{25} RR = 1.09, 95% CI: 1.05, 1.13; HN_{95th} RR = 1.10, 95% CI: 1.06, 1.14). Moreover, IHD (HN_{25} RR = 1.25, 95% CI: 1.21, 1.30; HN_{95th} RR = 1.24, 95% CI: 1.20, 1.29) showed the greatest risk among all 11 death causes. The estimated effect was lower for total RD (HN_{25} RR = 1.09, 95% CI: 1.07, 1.12; HN_{95th} RR = 1.12, 95% CI: 1.09, 1.14) than for CVD. The RR of senility mortality due to age-related physical disability related to hot nights was 1.16 (95% CI: 1.12, 1.21) for HN_{25} and 1.14 (95% CI: 1.10, 1.19) for HN_{95th}, and that of renal disease was 1.08 (95% CI: 1.03, 1.13) for HN_{25} and 1.04 (95% CI: 1.00, 1.09) for HN_{95th} (Table 1). Figure 2A shows the lag–response curves related to HN_{25} and Figure 2B shows HN_{95th} for all-cause and cause-specific mortalities. There had been no substantial difference in the shape of the lag responses by hot nights definitions considered, whereas the models of HN_{95th} were a bit more stable than those of HN_{25} because of the sufficient counts of hot nights. The estimated effects of hot nights on all-cause mortality appeared immediately and lasted for 2 wk. Similarly, the estimated effects of all cause–specific subgroups lasted for 2 wk, except the estimated effects of hot nights on renal disease, which lasted less than 1 wk. The mortality risks of CVD and its subdivision associated with hot nights were highest on lag day 0, whereas the mortality risks of asthma and renal disease were highest on later days (Figure 2). In addition, the all-cause mortality risks of hot nights showed the longest lag days for elderly (≥65 y old) people among the three age groups, whereas people younger than 15 y showed higher and more immediate effects (Figure S5).

Geographic Variation of the Hot Nights-Mortality Association

At the national level, the lag cumulative RRs for the impact of hot nights on all-cause mortality was 1.09 (95% CI: 1.08, 1.10) for HN_{25} and 1.10 (95% CI: 1.09, 1.11) for HN_{95th}. The strength of the association between hot nights and mortality varied among prefectures, and the geographic variation was notably larger for HN_{25} in comparison with HN_{95th} (Figures 3 and 4). Disparate magnitudes of prefecture-specific estimates were mostly observed in the northern region [Hokkaido (R1) and Tohoku (R2)]. Pooled regional estimates of HN_{25} were the highest in Hokkaido (R1; RR = 5.90, 95% CI: 2.21, 15.74) and Tohoku regions (R2; RR = 1.36, 95% CI: 1.06, 1.75), whereas those of HN_{95th} were the highest in the Tohoku regions (R2; RR = 1.15, 95% CI: 1.11, 1.18), and the lowest was in Hokkaido (R1; RR = 1.03, 95% CI: 1.00, 1.06). In other regions (R4–R8), estimates were close, and the trends were similar under the two definitions considered because prefecture-specific T_{thresh} for HN_{25} and HN_{95th} were close to each other (Table S2). The association between hot nights and mortality effects was larger in Tokyo (P13; R3; HN_{25} RR = 1.10, 95% CI: 1.08, 1.12; HN_{95th} RR = 1.10, 95% CI: 1.07, 1.13) and Osaka (P27; R5; HN_{25} RR = 1.11, 95% CI: 1.08, 1.13; HN_{95th} RR = 1.11, 95% CI: 1.09, 1.15) than their surrounding prefectures.

Table 1. Pooled RRs (95% CIs) for cause-specific mortality associated with hot nights (HN_{25} and HN_{95th}) estimated from a time-series quasi-Poisson regression with distributed lag models in Japan (1973–2015). Models were adjusted for the daily mean temperature, day of the week, seasonality, and the long-term trend.

	RRs (95% CI)	
Cause-specific mortality	HN_{25}[a]	HN_{95th}[b]
All-cause	1.09 (1.08, 1.10)	1.10 (1.09, 1.11)
CVD	1.17 (1.15, 1.19)	1.17 (1.15, 1.19)
IHD	1.25 (1.21, 1.30)	1.24 (1.20, 1.29)
CBVD	1.13 (1.11, 1.15)	1.13 (1.10, 1.15)
CH	1.09 (1.05, 1.13)	1.10 (1.06, 1.14)
CIN	1.14 (1.11, 1.18)	1.15 (1.12, 1.19)
RD	1.09 (1.07, 1.12)	1.12 (1.09, 1.14)
Pneumonia	1.08 (1.06, 1.11)	1.12 (1.09, 1.16)
COPD	1.11 (1.04, 1.19)	1.13 (1.06, 1.21)
Asthma	1.17 (1.06, 1.30)	1.11 (0.99, 1.25)
Renal disease	1.08 (1.03, 1.13)	1.04 (1.00, 1.09)
Advanced age	1.16 (1.12, 1.21)	1.14 (1.10, 1.19)

Note: CBVD, cerebrovascular disease; CH, cerebral hemorrhage; CI, confidence interval; CIN, cerebral infarction; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular diseases; HN_{25}, days on which the daily minimum temperature is ≥25°C; HN_{95th}, days on which the daily minimum temperature is ≥95th percentile of the daily minimum temperature of that prefecture during the study period (i.e., April–November 1973–2015); IHD, ischemic heart disease; RD, respiratory disease; RR, relative risk.
[a]HN_{25}: days on which the daily minimum temperature is ≥25°C.
[b]HN_{95th}: days on which the daily minimum temperature is ≥95th percentile of the daily minimum temperature of that prefecture during the study period (i.e., April–November 1973–2015).

We further conducted random-effects meta-regression analyses to investigate the heterogeneity of HN_{25} effects between prefectures. The RRs associated with HN_{25} per 1 standard deviation (SD) increase in each meta-predictor are shown in Table 2. Decreased AC prevalence corresponded to stronger effects from hot nights. Location information was significantly associated with RRs, and the heterogeneity between prefectures was explained the most by latitude among all meta-predictors, with an overall I^2 of 40.9%. The RRs were negatively associated with higher levels of mean, minimum, and maximum temperatures. None of the demographic and socioeconomic variables were statistically significant, and the residual heterogeneity changed very little in comparison with 56.2% of the model with no predictor. Though, the prefecture level could mask potential differences in vulnerability between socioeconomic groups occurring at the individual level. Cochran's Q tests for heterogeneity were significant for all prefecture-specific indicators as meta-predictors.

Within-Summer Variation in the Risk

Figure 5 shows the overall cumulative RRs predicted from the time-varying DLM for early and late summer, corresponding to middle of June and August, respectively (Excel Table S6). The higher RRs in early summer (corresponding to the middle of June) were observed in comparison with the late summer (corresponding to the middle of August) in all regions.

Sensitivity Analyses

We confirmed that the main model was conservative and stable regarding model parameter choices. Results were not statistically different in the sensitivity analyses that were additionally adjusted for RH (Table S4). The sensitivity of the results to alternative ways of setting the lag days at 14 and 28 in CB functions of hot nights and temperature was slight. The risk estimate in the model in which the maximum temperature was adjusted was not statistically

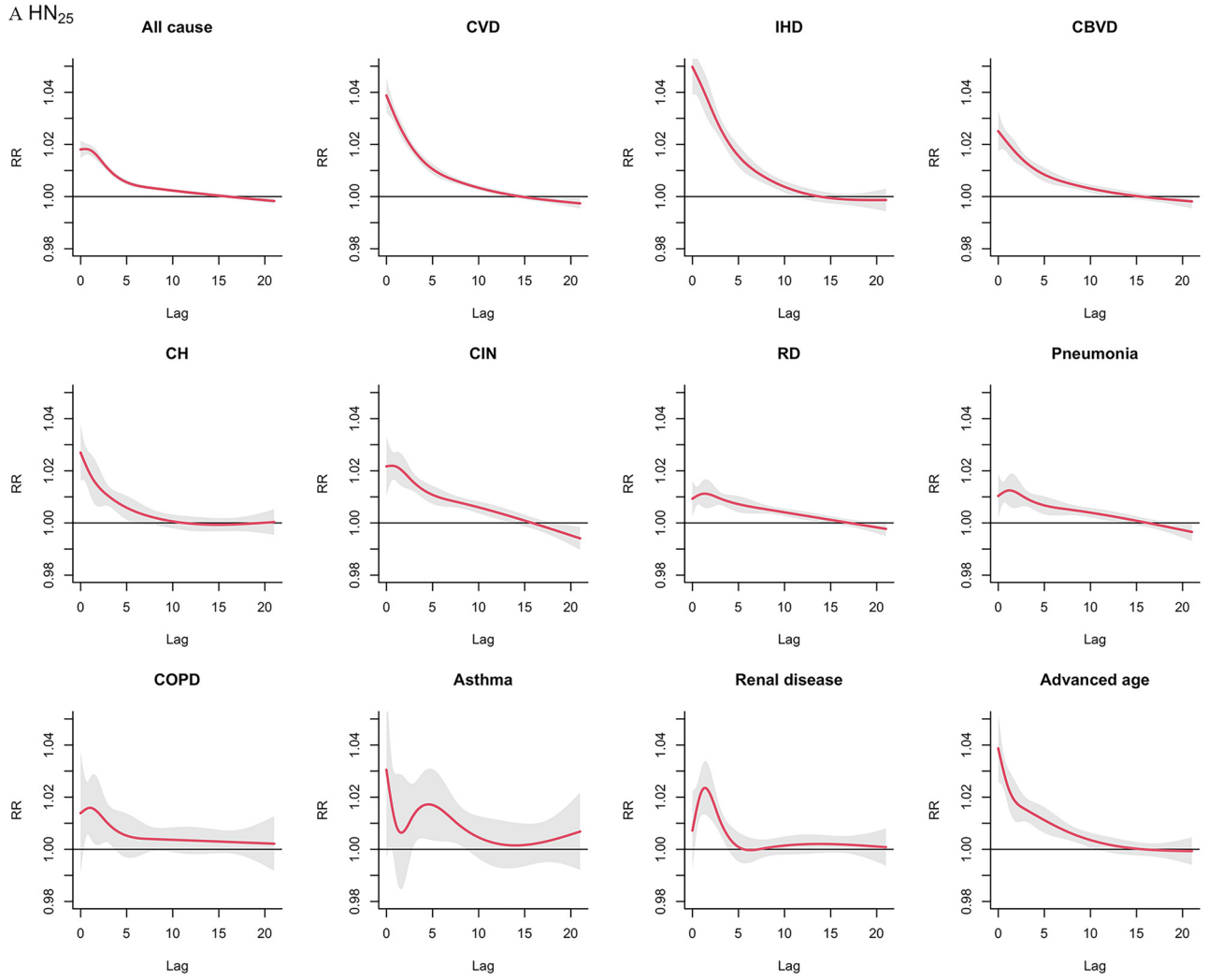

Figure 2. Lag structures in the effect of hot nights [(A) HN_{25} and (B) HN_{95th}] on daily cause-specific mortality estimated from a time-series quasi-Poisson regression with distributed lag models in 47 Japanese prefectures (1973–2015). Models were adjusted for the daily mean temperature, day of the week, seasonality, and the long-term trend. Solid lines on the curves correspond to estimates, and shaded areas are 95% CI. HN_{25}, days on which the daily minimum temperature is $\geq 25^{\circ}C$; HN_{95th}, days on which the daily minimum temperature is $\geq$95th percentile of the daily minimum temperature of that prefecture during the study period (i.e., April–November 1973–2015). Note: CBVD, cerebrovascular disease; CH, cerebral hemorrhage; CI, confidence interval; CIN, cerebral infarction; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular diseases; IHD, ischemic heart disease; RD, respiratory disease; RR, relative risk.

different from that in the main model in which the mean temperature was adjusted (Figure S6; Excel Table S4). Moreover, significant independent effects of hot nights on mortality were found when accounting for the heatwave variable in the model, suggesting that hot nights carry an additional risk of heat-related death (Figure S7; Excel Table S5).

Discussion

To the best of our knowledge, this nationwide, population-based epidemiological study over four decades is the first to comprehensively examine the association between hot nights and mortality in the Japanese population. We observed that hot nights were strongly associated with increased all-cause and 11 cause-specific mortality risks in Japan, and this association was found to be rather immediate and prolonged for a few weeks. Geographic variations in the associations were clear when the physiology-based threshold temperatures were considered, but it was less varied, especially in the northern regions when considering the community-based thresholds. Moreover, an overall hot night effect was evident, whereas the time-varying prediction suggested a greater effect of earlier exposures. The findings of this study have important implications for public health because current and future trends suggest that daily minimum temperatures are expected to rise faster than daily maximum temperatures, and the adverse health impacts of hot nights are conceivably predictable and preventable with specific public health actions.

In time-series of heat impact studies, conducting analyses stratifying cause-specific mortality and exploring the temporal lag pattern of associations between heat exposure and different disease outcomes aid our understanding of the possible mechanisms that induce heat-related health events and help prevent adverse outcomes of such events.[5,34] Previous studies postulated the causal relationship between heat exposure and impaired physiological functions, and there is substantial evidence of potential heat-related mechanisms initiating health problems. These mechanisms involve multiple physiopathology modifications, including changes in hormones, blood viscosity, blood pressure, heart rate, dehydration, and increased oxidative arterial damage and systemic inflammatory response.[35,36] Cause-specific analysis results confirmed that mortality due to all 11 causes was positively associated with hot nights, and different effect sizes and lag patterns of different disease outcomes were observed. Our results suggest

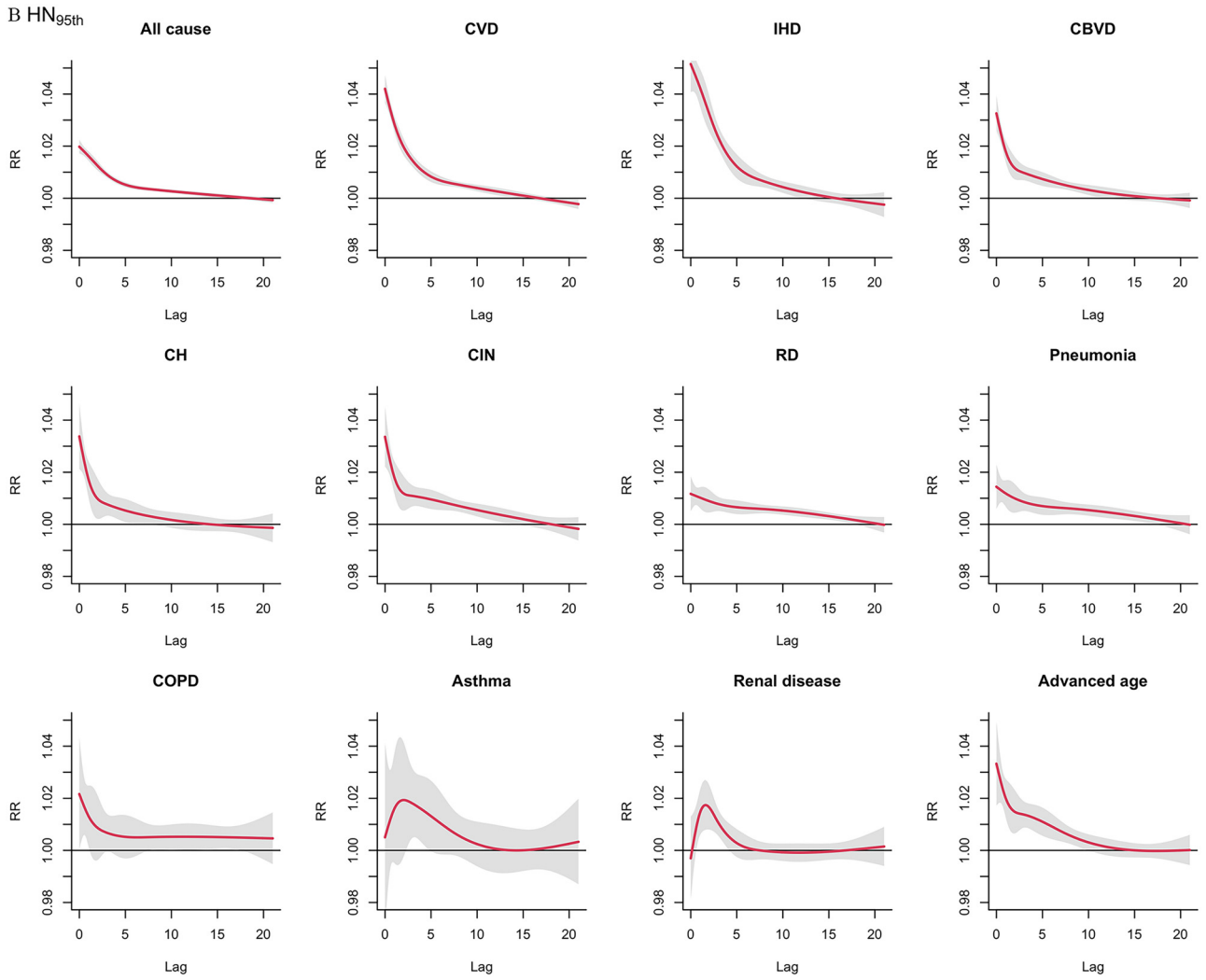

Figure 2. (*Continued.*)

that hot night effects on all-cause mortality appeared immediately and lasted for 2 wk, which is longer than the time in a multicountry study reporting that the heatwave effects on mortality were immediate and lasted 3–4 d in most countries, including Japan.[5] Moreover, a strong and immediate relationship between heatwave exposure and CVD has been reported in previous studies.[37,38] Similarly, there was an immediate increase in the estimated hot night effect on total CVD mortality on the same day of exposure and a decline in the following days in our study. The effects of hot nights lasted for 2 wk in our study, and this is also longer than the lag effect of high ambient temperature on CVD mortality in a prior study.[39] The mortality related for all four CVD subdivisions was positively associated with hot nights, and the differences in estimates might be partly explained by different potential physiopathological mechanisms among the CVD subdivisions. Especially, IHD showed the strongest association because it is related to dehydration, which can be accelerated during nighttime when people do not usually hydrate. In contrast with earlier findings of heat-related RD mortality effects being higher than heat-related CVD effects,[40] the hot nights–related RD mortality effects were weaker than the hot nights–related CVD effect. The mortality of all three RD subdivisions, pneumonia, COPD, and asthma was positively associated with hot nights, which presented a much longer effect on COPD deaths than on other RD subdivisions. Renal deaths were also considered in this study because it is plausible to suspect that dehydration and hyperthermia cause kidney dysfunction.[41] We found that the significant hot nights effects on renal deaths lasted up to 5 d, which was the shortest among the 11 causes of deaths that we considered.

Moreover, a prior study noted that population subgroups, particularly elders, are vulnerable to heat-related mortality.[42] Our elder death results suggest that hot nights may increase elders' mortality risk, and the association between hot nights and the aforementioned risk was strong, immediate, and lasted 2 wk. The relationship between hot nights and hospitalizations would provide a more direct understanding of a causal effect. In two studies, Liss et al. and Liss and Naumova examined the association between hot night temperatures and heat-related admissions and provided evidence for the high vulnerability of older adults to heat stressors.[43,44] Biological mechanisms and possible behavioral explanations have been hypothesized for the association between mortality among elders and hot nights. Thermoregulatory functions are likely to decrease with age, and shifted blood flow from vital organs underneath the skin continues when high body temperatures do not fall, putting increased stress on organs and impeding thermoregulation.[45] Dehydration is another possible factor causing this strong association and is a problem frequently experienced by elders.[46] Age-related changes in total body water, thirst perception, and renal concentrating ability probably predispose patients to dehydration.[47] Elderly people tend not to drink before and during sleep to avoid

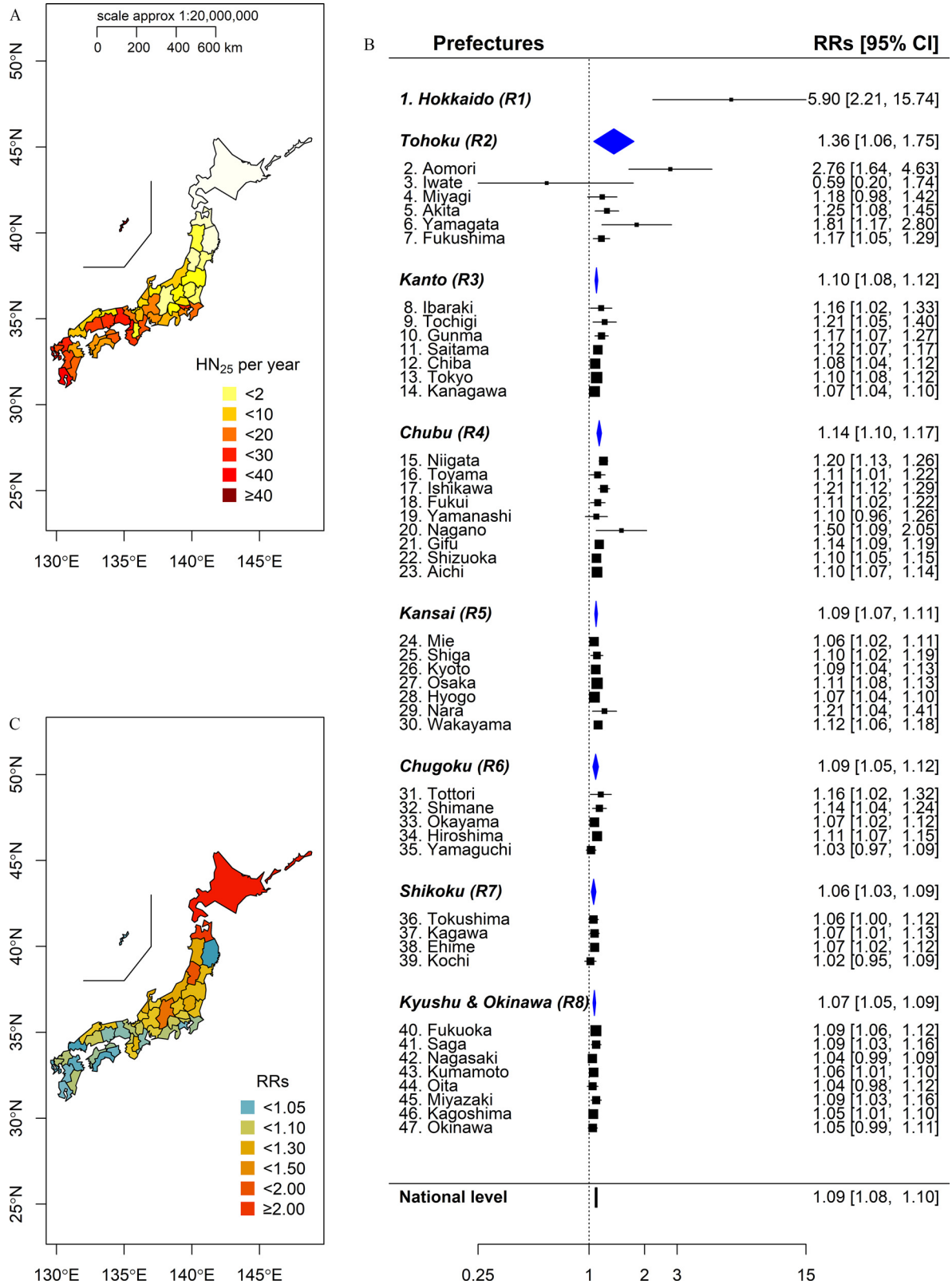

Figure 3. Geographic variations in HN_{25} events and risks of all-cause mortality estimated from a time-series quasi-Poisson regression with distributed lag models in 47 Japanese prefectures (1973–2015). Models were adjusted for the daily mean temperature, day of the week, seasonality, and the long-term trend. (A) The average number of HN_{25} events per year; (B) Cumulative effects of HN_{25} on all-cause mortality. Prefecture-specific and pooled, including regional and national, RRs (95% CIs) associated with HN_{25}. Points correspond to estimates, and whiskers reflect 95% CIs. Weight is presented as the size of each estimate point; (C) Geographic variations in the estimated prefecture-specific RRs. Note: CI, confidence interval; HN_{25}, days on which the daily minimum temperature is ≥25°C; RR, relative risk.

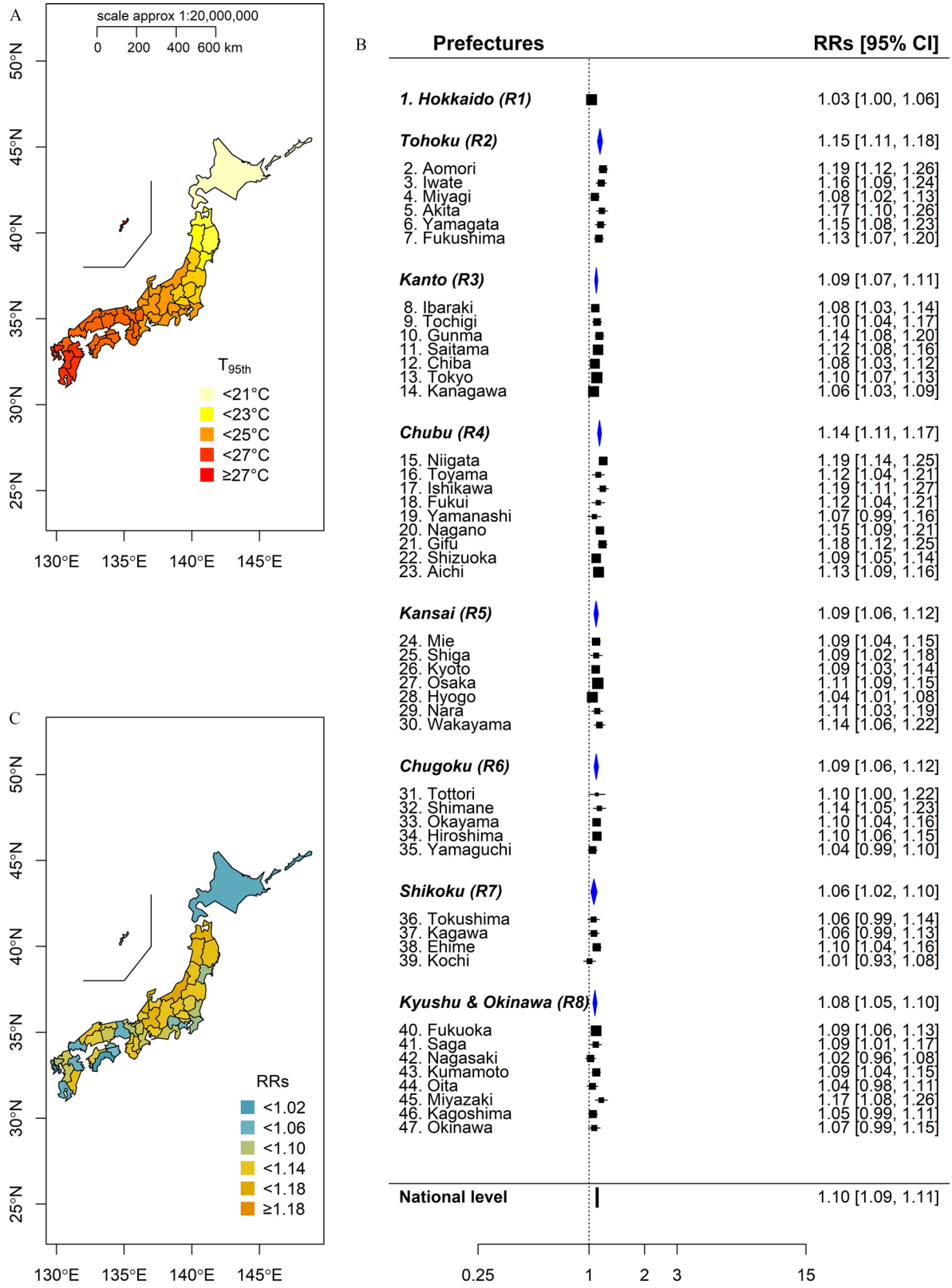

Figure 4. Geographic variations in HN_{95th} events and risks of all-cause mortality estimated from a time-series quasi-Poisson regression with distributed lag models in 47 Japanese prefectures (1973–2015). Models were adjusted for the daily mean temperature, day of the week, seasonality, and the long-term trend. (A) The average number of HN_{95th} events per year; (B) Cumulative effects of HN_{25} on all-cause mortality. Prefecture-specific and pooled, including regional and national, RRs (95% CIs) associated with HN_{95th}. Points correspond to estimates, and whiskers reflect 95% CIs. Weight is presented as the size of each estimate point; (C) Geographic variations in the estimated prefecture-specific RRs. Note: CI, confidence interval; HN_{95th}, days on which the daily minimum temperature is ≥95th percentile of the daily minimum temperature of that prefecture during the study period (i.e., April–November 1973–2015); RR, relative risk.

Table 2. Associations between prefecture-specific indicators and hot night estimates. RRs (95% CIs) per 1 SD increase calculated from a univariate meta-regression model ($n = 47$). Residual heterogeneity was tested to report the Cochran Q test and I^2 statistic.

Meta-predictors	Mean ± SD	RR per 1 SD (95% CI)	Cochran Q-test p-value	I^2
Air conditioning				
AC[19] (%)	71 ± 22.85	0.9760 (0.9534, 0.9992)*	<0.0001	56.8
Climate[15]				
Tmax (°C)	19.62 ± 2.24	0.9596 (0.9440, 0.9755)*	0.0009	44.1
Tmean (°C)	15.13 ± 2.34	0.9627 (0.9482, 0.9774)*	0.0011	43.5
Tmin (°C)	11.23 ± 2.54	0.9686 (0.9549, 0.9825)*	0.0003	46.6
Location[22]				
Latitude	35.38 ± 2.62	1.0203 (1.0095, 1.0312)*	0.0026	40.9
Longitude	136.04 ± 3.70	0.9760 (0.9534, 0.9992)*	0.0001	50.8
Demographic[27]				
Population	2,631,252.37 ± 2,467,548.34	1.0011 (0.9928, 1.0094)	<0.0001	56.7
Elderly (%)	24.77 ± 2.65	0.9979 (0.9876, 1.0084)	<0.0001	56.8
Female (%)	51.58 ± 0.97	0.9926 (0.9839, 1.0014)	<0.0001	55.6
Socioeconomic				
Outpatien[28]	1,218.55 ± 228.2	0.9974 (0.9864, 1.0085)	<0.0001	57.1
EPI[29]	0.47 ± 0.2	1.0031 (0.9947, 1.0116)	<0.0001	56.4
Urbanization[30]	6.33 ± 11.08	1.0001 (0.9923, 1.0079)	<0.0001	56.8

Note: The mean and SD were calculated over 47 prefectures using the prefecture-specific average annual statistics. AC, air conditioning; CI, confidence interval; EPI, economic power index; RR, relative risk; SD, standard deviation; Tmax, maximum daily mean temperature; Tmean, average daily mean temperature; Tmin, minimum daily mean temperature. *$p < 0.05$.

sleep disturbance and urination problems.[48] Moreover, Japanese elders tend to use air conditioners during their sleep less than young people for power saving[49] and believe that nighttime air conditioner usage is bad for their health.[50] These hot night risks are likely to increase rapidly in the near future with temperature rises due to climatic change and the continued population aging in Japan, which has the world's oldest population, with 28.4% of its population over the age of 65. This percentage is expected to increase to 35.3% by 2040,[51] with the public fiscal constraints imposed by aging populations making it more challenging for governments to finance measures to mitigate and adapt to the impacts of climate change.

Physiology-based thresholds (absolute values of used measures) or community-based thresholds (relative values) are typically used to set the threshold temperature for heat in epidemiological studies.[52] We used both thresholds in our analyses; a physiology-based threshold helps aid our policymakers intuitively because an official definition of hot nights uses 25°C under current law for the Japanese population. The physiology-based threshold varies by location (e.g., 20°C in Europe).[53] Mortality risks associated with hot nights, defined by an absolute temperature, were higher in northern Japan where hot night events were rare, and the risks were lower in southern Japan, where hot night events were more common. The observed trends are in line with findings from heatwave studies in Japan.[54] However, these findings need to be interpreted with caution when extrapolating them to other regions because it has been suggested in a multicountry study that, geographically, heatwave effects were greater in moderately cold and hot areas than in cold and hot areas.[5] Our further meta-analyses confirmed that temperatures and location information could modify the hot nights–mortality association. People living in areas where high temperatures are not generally experienced are more likely to be susceptible to heat events, and those living in areas with high temperatures appear to be more adaptable to heat.[7,55] Increased temperature and lower latitude (warmer regions) corresponded to weaker effects from hot nights, which might be attributed to adaptation and acclimatization. Community-based threshold, on the other hand, is a measure of population tolerance to its local climates because it describes historic regional adaptations to temperatures that were normal at each location.[56] We observed lower community-based thresholds in the northern part of Japan and higher thresholds in the southern part, closer to the equator. The observed geographical trend of the hot night risk computed using the relative temperature was similar to the result using the absolute temperature, except for several northernmost prefectures. This observation may be because of the large difference between the relative and absolute thresholds. Differences in relative thresholds across the prefectures are likely to reflect not only the long-term physiological acclimatization but also social betterment, such as health care system and housing improvement, and other behavioral and cultural factors.

Furthermore, it is noticeable that hot nights and risks were more abundant and higher, respectively, in densely populated prefectures, such as Tokyo (P13; R3) and Osaka (P27; R5), than in surrounding areas. The findings of studies in the United States, Europe, and China suggest that urban mortality was more sensitive to heat than suburban and rural mortality.[21,57–59] Hot nights in metropolitan areas can be elucidated using the influence of the urban heat island (UHI) phenomenon, a common phenomenon in which surface temperatures are higher in urban areas than in surrounding rural areas. Human-induced land conversion has reduced albedo, and artificial materials store more radiation energy in the daytime and cool insufficiently in the nighttime.[60] The atmospheric UHI phenomenon reaches its highest intensity at night[61]; heat is trapped on low levels lingering in and between buildings and cannot be released.[62] This phenomenon is observed and certainly presented in metropolitan areas in Japan. Because the highest yearly temperature is apparently particularly accelerated in most megacities around the globe,[63] the number of hot nights is also expected to increase in urban areas.[64] In the Tokyo (P13; R3) prefecture, with a population of more than 13.5 million people (Table S1), the average number of hot nights increased from 23 d per year (1973–1995) to 32 d per year (1996–2015). Similarly, in the Osaka (P27; R5) prefecture, with a population of 8.8 million people (Table S1), the average number of hot nights increased from 31 d per year (1973–1995) to 41 d per year (1996–2015). Thus, the combined effect of hot nights and increases in the number of urban residents means that heat stress in urban areas is likely to become an even more critical issue in the future. Future increases in minimum temperature, as predicted by various climate change scenarios,[1,8] will result in an increase in the risk of hot nights in particular in urban areas.

Regarding the within-season variation in mortality risk associated with hot nights, our findings indicated that population susceptibility was reduced in late summer in comparison with that in earlier summer. The present results are consistent with findings

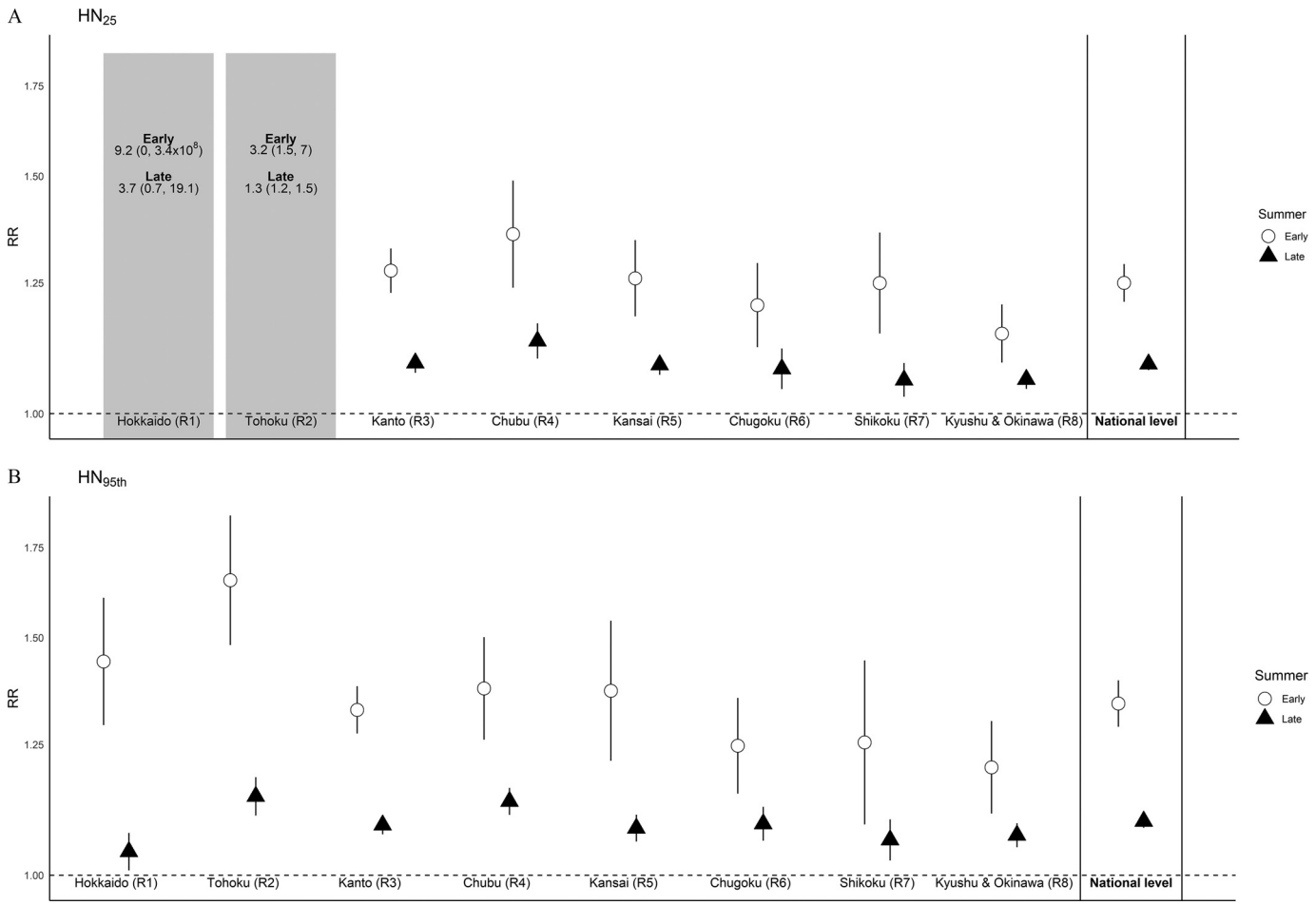

Figure 5. Hot night [(A) HN_{25} and (B) HN_{95th}] effects on all-cause mortality predicted for early (corresponding to the midpoint of June) and late summer (corresponding to the midpoint of August) period from a time-varying distributed lag models in eight regions of Japan (1973–2015). Models were adjusted for the daily mean temperature, day of the week, seasonality, and the long-term trend. The white circles correspond to estimates for early summer and the dark triangles for late summer. Whiskers reflect 95% CIs (See Excel Table S6 for corresponding numerical data). Note: CI, confidence interval; HN_{25}, days on which the daily minimum temperature is $\geq 25^{\circ}C$; HN_{95th}, days on which the daily minimum temperature is $\geq$95th percentile of the daily minimum temperature of that prefecture during the study period (i.e., April–November, 1973–2015); RR, relative risk.

from previous studies assessing changes in mortality risk associated with heat during summer.[6,32,65] There are several possible explanations for this result. The deaths of susceptible individuals during hot nights in early summer leave a reduced pool of susceptible individuals later in the summer (i.e., mortality displacement). In addition, the population can physiologically acclimatize (e.g., more efficient sweating) and behaviorally adapt (e.g., use of AC) to a warmer climate to some extent simultaneously.

AC is a commonly cited behavioral adaptation.[20,21] We also found that the association between hot nights and mortality was stronger for prefectures with a lower AC prevalence, decreasing the adaptive capability against heat exposure. However, addressing this issue and the issue of heat more broadly poses a difficult challenge for policymakers. In the short term, using AC offers protection against heat impacts on health. However, AC puts more heat-trapping gases into the atmosphere, consequently resulting in more hot nights. This feedback loop will continue unless the aforementioned issues are overcome with ecological actions, such as energy source transformation, which require not only advanced green technology but political support.

Japan's climate adaptation strategy is being widely implemented. In the health sector, much attention currently focuses on the maximum and mean temperatures in relation to adaptation to heat stress. People have a lower level of risk preparedness against heat at night than during the day because they are sleeping, sometimes in poor conditions. Our results showed an independent effect of excess mortality, supporting our hypothesis that there is an added hot night effect beyond mean temperature and heatwave effects. The findings of this study made clear that attention should also be paid to daily minimum temperature in setting up public health communications and that reductions in health burdens from hot nights are as important as similar reductions in daytime heat for mitigating heat-related health problems.

There are several limitations to this study. First, accidental mortality was not separately considered, and hot nights might indirectly affect accidental mortality. Hot nights might lead to sleep problems, and these lead to accidents; sleeping problems were associated with an increased risk of a work injury,[66] and sleeping-pill users have an increased risk of road traffic accidents.[67,68] Second, because we used the mortality data, clinical variables such as multimorbidity were not considered. Third, this study was conducted in Japan only, meaning our results should be interpreted cautiously because they may not be applicable to other areas. Further investigations, including multiple locations, are necessary to fully elucidate the health impact of hot nights due to climate change. Last, this study focused on the overall effect of hot nights on mortality to understand whether hot nights increase the risk of death and increase adverse effects among those who are at increased risk in general, because there is very limited

information on the health risks of hot nights. However, understanding potential changes in detected effects over time could be of value for prediction, and many factors related to population resilience are time-sensitive. Therefore, further research should be undertaken to investigate changes in population susceptibility to hot nights over time.

Conclusion

In our study, exposure to hot nights was associated with a broad range of cause-specific mortality in the Japanese population. The geographical disparity in the climate conditions and mortality risks of hot nights were observed, indicating the importance of developing area-specific adaptation strategies and local awareness plans for risk prevention that can serve as a basis for policymaking to mitigate climatic change and reduce the corresponding health effects. This study also demonstrated that hot nights have health impacts in addition to daily mean temperature and heatwaves, indicating that minimum temperatures are also an important consideration when developing heat-health warning systems, highlighting the need for more research on the potential effects of hot nights.

Acknowledgments

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