Assessing the associations of temperature and mortality in the Philippines

(フィリピンにおける死亡に対する気温の影響を評価)

A PhD Thesis Submitted in Partial Fulfillment for the

Requirements of Doctoral Program in Human Care Sciences

Xerxes Tesoro Seposo, PgDENRM, MENRM, MPH

PhD Candidate

Professor Yasushi Honda, MD, PhD

Thesis Adviser

February, 2017

Contents

Acknowledgements

For more than three years in the making, this thesis will not be possible if not for the people who were there to support me all the way. Let me start with thanking my three professors, Prof. Ichiro Okubo (大久保　一郎), Prof. Masahide Kondo (近藤　正英), and Prof. Yasushi Honda (本田靖). I am forever indebted to all the three professors have guided me all throughout my years in Japan ever since my research student year.

I would like to especially thank my Thesis Adviser, Prof. Honda, for giving me a chance to be in his laboratory for all these years, and supporting me with the things I needed, to equip me for my PhD life. I could have never asked for anymore greater than the laboratory environment that I have now, and the guidance from the professors. I would also like to extend my thanks and appreciation to my panel reviewers for providing insightful comments for the betterment of this manuscript.

I would like to thank my laboratory colleagues to whom I owe my sanity for all these years. Let me recount the people who have shared this journey with me ever since my research student year: to Momoko-san (桃子さん), Shina-san (椎名さん), Matsubayashi-san (松林さん), Hoshi-san (星さん), Nishiyama-san (西山さん), Deni-san, Shin-kun, Jung-kun, Dang-san, Ma-san (馬さん), Jesa-san, Mamata-san, Sib-san, Jade-san, Oikawa-san (及川さん), Tanya-san, Okayasu-san (岡安さん), Ichinose-san (市瀬さん), Maeda-san (前田さん), Murasawa-san (村澤さん), and to an extended laboratory colleague, Araki-san (荒木さん). Likewise, I would like to extend my heartfelt gratitude to the Ozawa-san (小澤さん), who was always there to constantly and religiously remind me of the things I needed for my PhD progress and other related matters.

I would like to thank my Tsukuba family, both within Tsukuba University and to those from the Tsukuba Catholic Church. I would like to acknowledge my friends who, despite my character, were able to withstand me all these years; to Chitho, Leslie, Arvin, Grace, Ate Gwen, Kuya Julius, Ate Caryn, Basti, Indy, Jake, Bingbong, Ate Val, Kuya Angelo, Cas, and to the other past and present Filipino Association of Scholars in Tsukuba members. I would like to give special mention to Ma'am Cherry Ballescas for introducing me to the Church. Likewise, I would like to thank my TCC choir family for being so active during Sundays and any other pertinent outings.

I would also like to thank my Barkada back home, who were always there to remind me to enjoy life and be happy. I would like to also thank my family for being with me in this journey. Thank you, Papa, Mama, Toto, and Nene, for being there regardless of the ample time that I can render. Thank you for the never-ending trust and prayers, I can truly feel your support from afar. I will not be here if not for your moral and emotional support. I would also like to thank my beloved, Aden, for being my prayer warrior through rough times. Thank you for the unconditional love.

Lastly, I would like to dedicate this thesis, and even my PhD, to God, who has given me all the strength to conquer the trials I have faced through the years. He was there all the time, and guided me to the right path in achieving my goals. He let me meet great people, great friends, and allowed me to lean on to my family more. His presence outshines the sad moments of my life, thereby leading me to a blessed path.

Thank you all for believing in me, and this is all for you, and of course for the glory of God.

List of Tables

List of Figures (1)

List of Figures (2)

List of Figures (3)

Executive Summary

This PhD thesis is structured into seven (7) chapters, with each chapter complementing each other to have a coherent flow of understanding as to the objectives of this thesis. The studies are linked to each other with the first study being the baseline, while the succeeding studies as innovations, which tackle different aspects of the temperature-mortality relationship associations.

This thesis was able to successfully assess the associations of temperature and mortality in the Philippines using state-of-the art environmental epidemiology modeling techniques. The results of the respective studies, and the overall goal of the thesis can either be taken separately or as a whole. The key findings of the studies are summarized in the last chapter, which highlights the following: 1) risks observed in the extreme temperatures, particularly in the extreme high temperatures, 2) various populations experience different levels of risk, and 3) mean temperature is a major contributor to the risk.

By assessing the relationship of temperature and mortality, we were able to profile the factors which needs more focus, and were able to determine the various susceptibilities of a specific population with respect to the mean temperature and the other temperature indices.

CHAPTER 1: Introduction

1.1. Philippine climate and demography

The Philippines is the second largest archipelago in world, which consists of 7,107 islands with a land area totaling to more than 30M hectares (Cinco et al. 2014). As of 2010, it has a population of 92.3 million with an estimated growth rate of 1.9% per year (WHO and DOH-Philippines 2012). The country is made up of political local government units of provinces, cities, municipalities and barangays (WHO-WPRO 2011). There are 80 provinces, 138 cities and 1,496 municipalities and half the population (50.3%) live in urban areas, and of that, 44% live in slums (WHO and DOH-Philippines 2012). Lying in the Pacific Ring of Fire and the typhoon belt, the country is frequently visited by typhoons, and experience occasional earthquakes and other natural calamities.

Located near the equator, the country has two distinct seasons; rainy and dry (Tolentino et al. 2016). The dry season starts from December to May, which can further be subdivided into cool dry season (December to February) and hot dry season (March to May), while the rainy season is from June until November. The country experiences torrential rains during the rainy season, and with a year-round annual average rainfall summing up to 2000 mm (Cinco et al. 2014). Due to the increasing number of typhoons and the intensity of the extreme events associated with cyclones and flooding, the Philippines has been identified as one of the most vulnerable nations impacted by climate change (Villafuerte et al. 2014).

In response to the burgeoning problems related to climate change, both the Senate and the House of Representatives of the Philippines in Congress, ratified by the President, have enacted the Republic Act No. 9729, which created the Climate Change Commission (RA9729 2009). RA 9729 has embodied the previous agreements pertaining to climate change, such as the United Nations Framework Convention on Climate Change and Hyogo Framework. The commission was tasked to formulate a National Climate Change Action Plan which include, but not limited to the following:

> *(a) Assessment of the national impact of climate change;*
>
> *(b) The identification of the most vulnerable communities/areas, including ecosystems to the impacts of climate change, variability and extremes;*
>
> *(c) The identification of differential impacts of climate change on men, women and*
>
> *children;*
>
> *(d) The assessment and management of risk and vulnerability;*
>
> *(e) The identification of GHG mitigation potentials; and*
>
> *(f) The identification of options, prioritization of appropriate adaptation measures for joint projects of national and local governments.*

Ultimately, climate change is affecting all sectors of society, both domestically and globally, and has been so through the years (Portier et al. 2010). The current international frameworks, supported by the national mandates have be some of the few driving forces in mitigating its effect the society and on the immediate environment. Of the few aspects, whereby climate change has a debilitating effect, it is on human health. Efforts to frame the effects of climate change on health and its integration into the health system have been done at a general level, and is a continuous and developing effort to fully capture the extent of such effects.

1.2. Philippine health system

The country's health system, which was originally managed by the Department of Health (DOH), has been decentralized ever since the implementation of the Local Government Code of 1991, which transferred the management of the health services to the Local Government Units (LGU), leading to a decentralized and fragmented health service delivery (WHO-WPRO 2011; WHO and DOH-Philippines 2012). Even though the health services are decentralized, DOH, through its regional offices and provincial extensions, extend support towards the local units in terms of service or in kind. Numerous reforms have been introduced to the health system through the years, and likewise are programs which embody the commitment of the national government to international agreements affirmed in achieving the common goals; such as the recently concluded millennium development goals (MDG) and the current mandate of support to the sustainable development goals (SDG).

One of these initiatives has been linked towards addressing the impact of climate change through the recent COP21 commitment, as well as the UN SDGs. In the frameworks of SDGs 3 and 13, health and well-being together with climate action, have shown that health and climate change can be linked together. The success of the SDGs can't be achieved alone by solely sufficing a single goal, but to work across goals and find a common ground (ICSU and ISSC 2015). In such essence, we can address the impending health problems by looking through an environmental lens.

In response to this global goal, DOH through its environmental health program, devised a national roadmap, known as the Philippine National Environmental Health Action Plan

(NEHAP), which plans to prevent illnesses, either through management of the environment or through changing behaviors, which consists of interventions that prevent the generation of agents, vectors and/or risk factors (DOH 2010). The NEHAP focused on eight (8) key areas, namely: toxic and hazardous substances, air, water sector, sanitation sector, food safety, occupational health, solid waste, and climate change and health.

In the NEHAP roadmap, there is no explicit objective with regard how to address the climate change and health component. According to the NEHAP, "*the country has not yet fully appreciated the strategies to mitigate climate change related health impacts. Roles and responsibilities need to be further defined and resources have to be allocated to support climate change related initiatives. More studies have to be made specially on emerging diseases and* ***to provide evidence based policy advocacy on the burden of health impacts of climate change****.* ***The disease surveillance mechanisms and data collection systems need to be enhanced to factor in the correlation between climate change and health***" (DOH 2010). From this point on, efforts have been done to address these issues in line with either the global roadmap and/or that of the national framework in the Philippines.

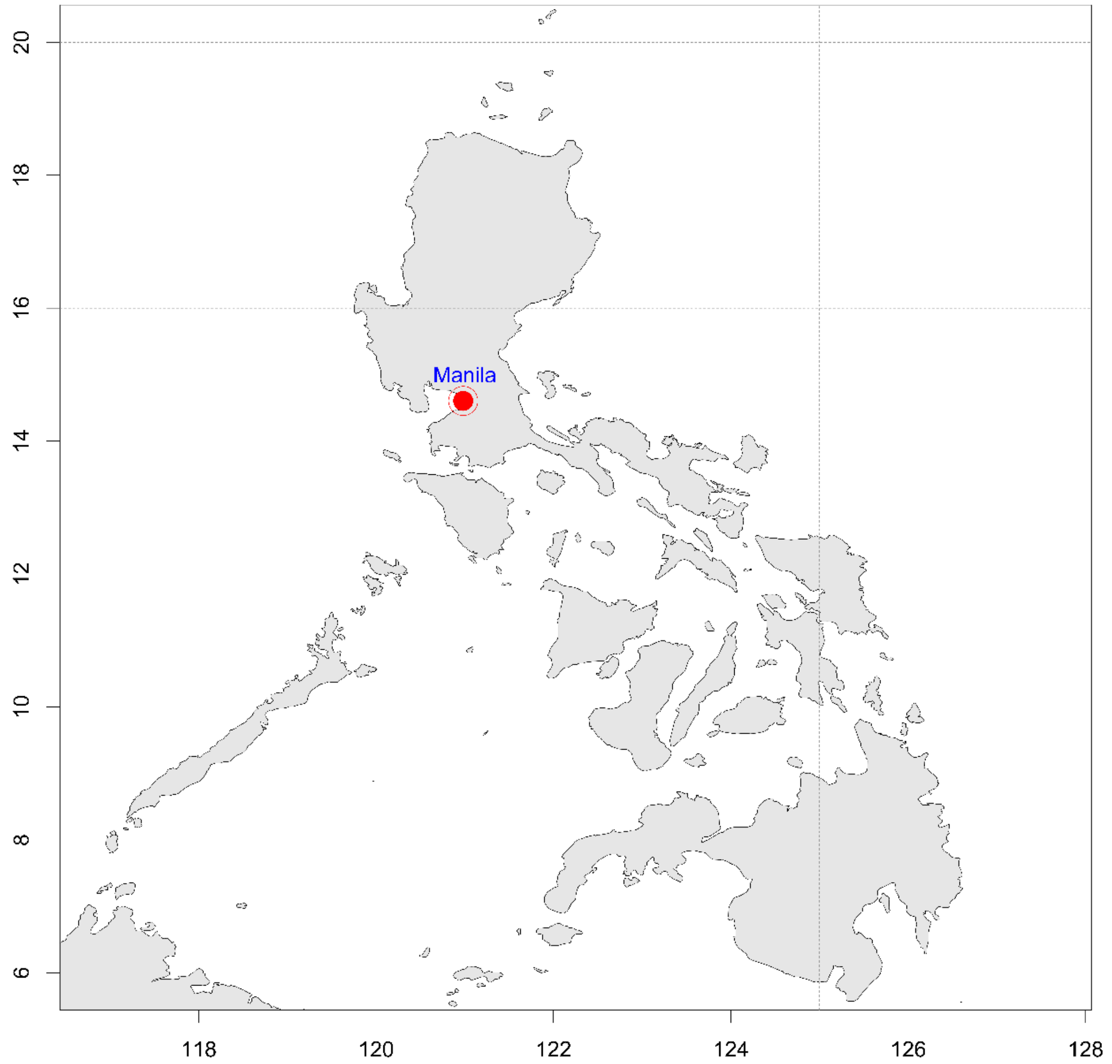

Figure 1. Map of the Philippines and its capital, Manila City

1.3. Review of Related Literature

1.3.1. Temperature-mortality Relationships

Multiple studies have explored the effects of temperature on mortality/morbidity in different cities of various countries across the globe (Gasparrini et al. 2015; Guo et al. 2014a). With the current progress in this field, this chapter is dedicated to the systematic review of the temperature-mortality studies. We used PubMed, a journal database, to search for the related literature using the following keywords: “temperature”, “mortality”, and “morbidity”, which yielded 402 studies. From 402 studies, we further streamlined the studies and applied an exclusion criterion which specified words to be used for the exclusion, as seen in Figure 2, leaving us with 288 studies. Most of the studies were from Asia (n=109), followed by Europe (n=57), and North America (n=42). However, we were not able to classify some of the studies (n=64) due to the lack of access to the journal. On the other hand, reviews and global studies summed up to eight (8), which implies that most of the studies are still city- or country-specific.

Figure 4 shows an imbalance about the profiling of risks with respect to the climate type, wherein most of the studies carried out were from temperate cities/countries (n=165), which only means that there is a knowledge gap with regard to the risks in a tropical setting. There are much to understand about these factors, and the past research provides a platform to the new directions in which this current thesis paper is aligned; to profile the risks in a tropical setting, specifically in the cities of the Philippines.

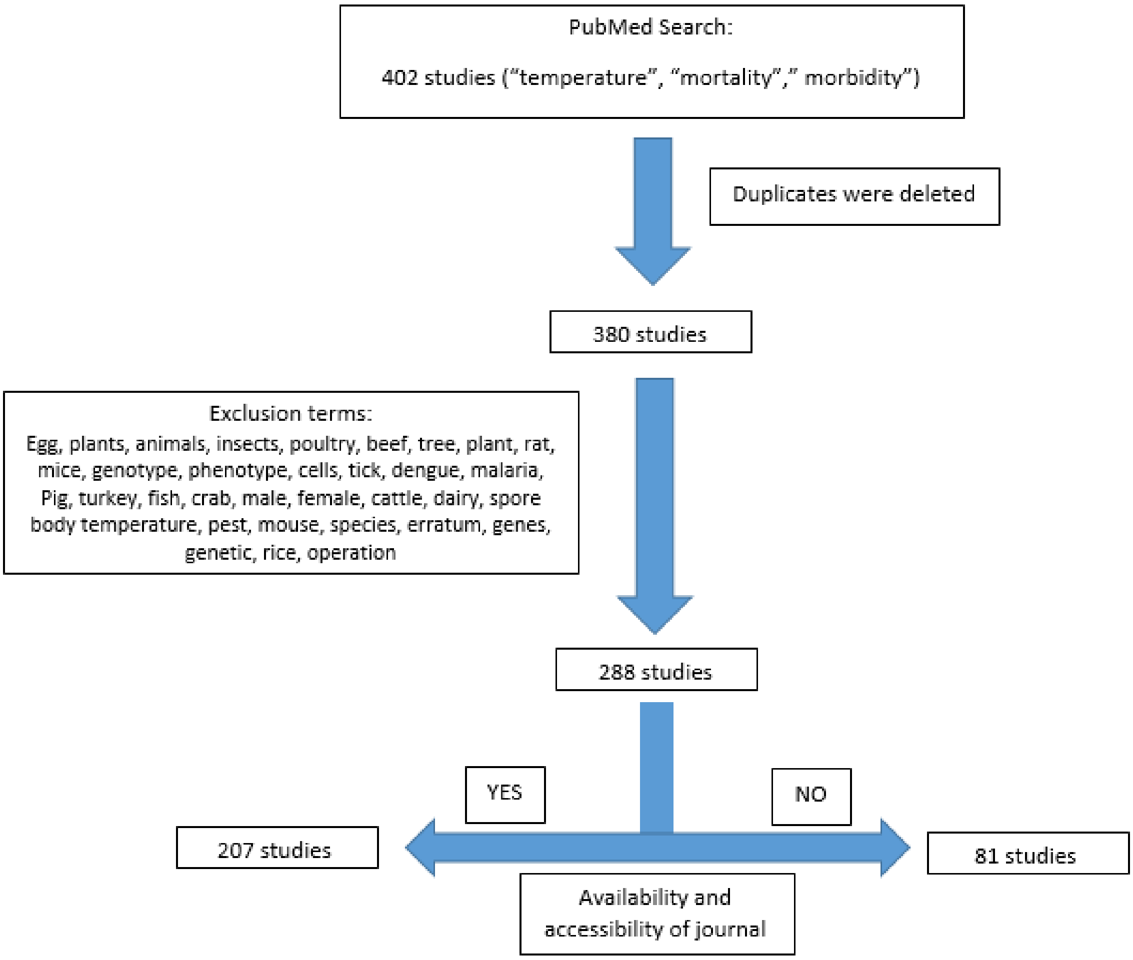

Figure 2. Schematic diagram of the search protocol

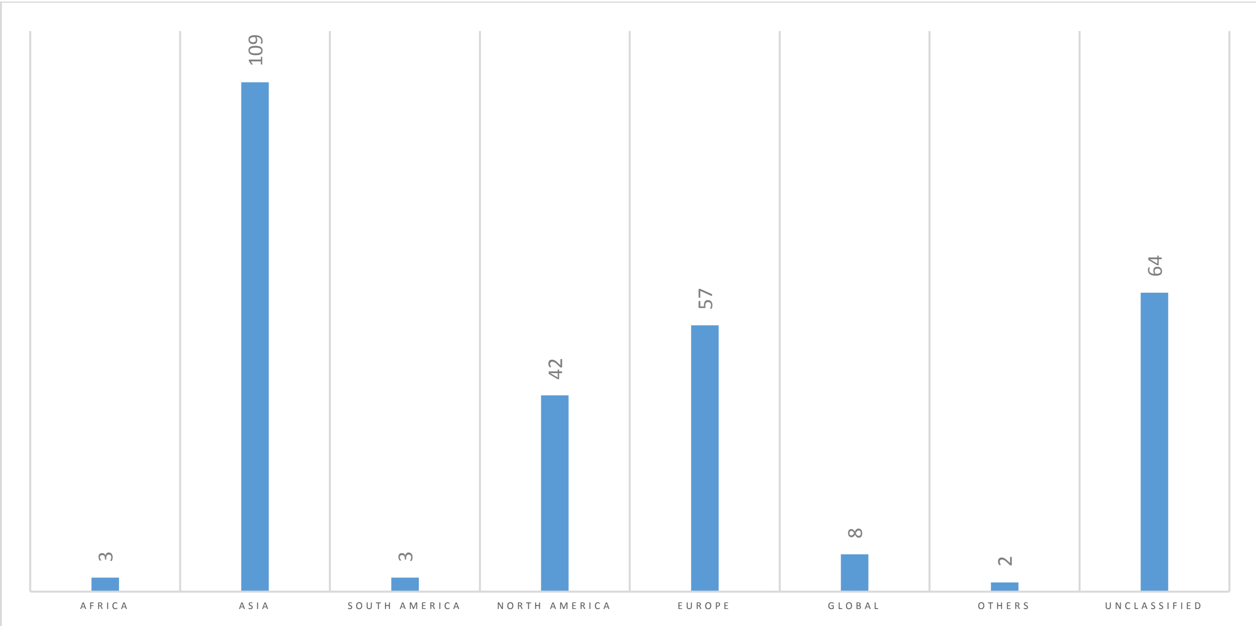

Figure 3. Distribution of the studies based on the region

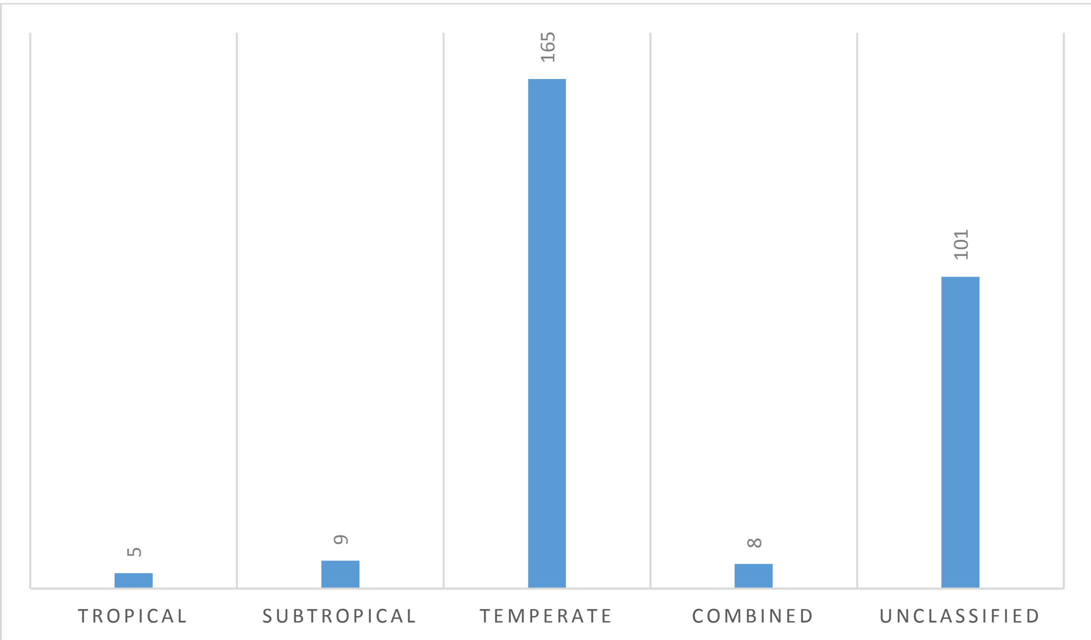

Figure 4. Distribution of studies based on the climate type

1.3.2. Techniques used in Temperature-mortality relationships modeling

In the previous sections, we have discussed the current Philippine environmental health situation and the need for more studies to document the risks in a tropical setting. In the field of temperature-mortality risk determination, there are numerous methods used to measure the risk such as, but not limited to: case-crossover (n=85) (Basu et al. 2005; Basu and Ostro 2008), traditional generalized linear models (n=15) (Kim et al. 2011; Likhvar et al. 2011), distributed lag model (n=10) (Goodman et al. 2004), distributed lag non-linear models (n=58) (DLNM) (Armstrong and Gasparrini 2012; Gasparrini et al. 2010; Gasparrini 2011; Gasparrini et al. 2012; Gasparrini and Armstrong 2013) and other techniques (n=124), which we were not able to document due to either lack of accompanying documentation for verification, or a combination of techniques, usually in multi-level analyses.

DLNM, aside from the "other" component, has been popularly used ever since its methodological introduction in 2010 (Gasparrini et al. 2010). According to Gasparrini et al. (2010), DLNM "*provides a flexibility in which the effects can vary simultaneously both along the space of the predictor and in the lag dimension of its occurrence*". Ever since 2010, DLNM has been popularly used, as seen in Figure 6. With the flexibility of DLNM and its viability for usage, we used mostly DLNM in our studies and tweaked them depending on the subject of interest. For further reading of the methodological specifications and parameterizations for the model, we invite the readers to explore Gasparrini et al. (2010) and Gasparrini (2011). For the study-specific parameterizations, we have explicitly defined them in the specific sections' methods, and have structured them to be standalones.

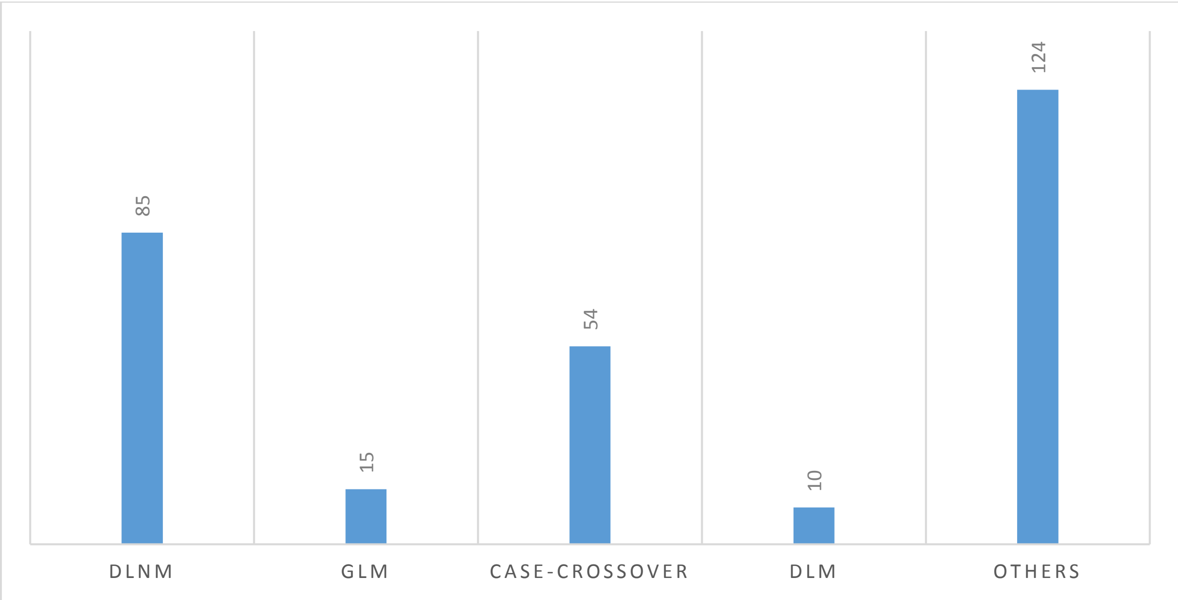

Figure 5. Modeling techniques by popular usage

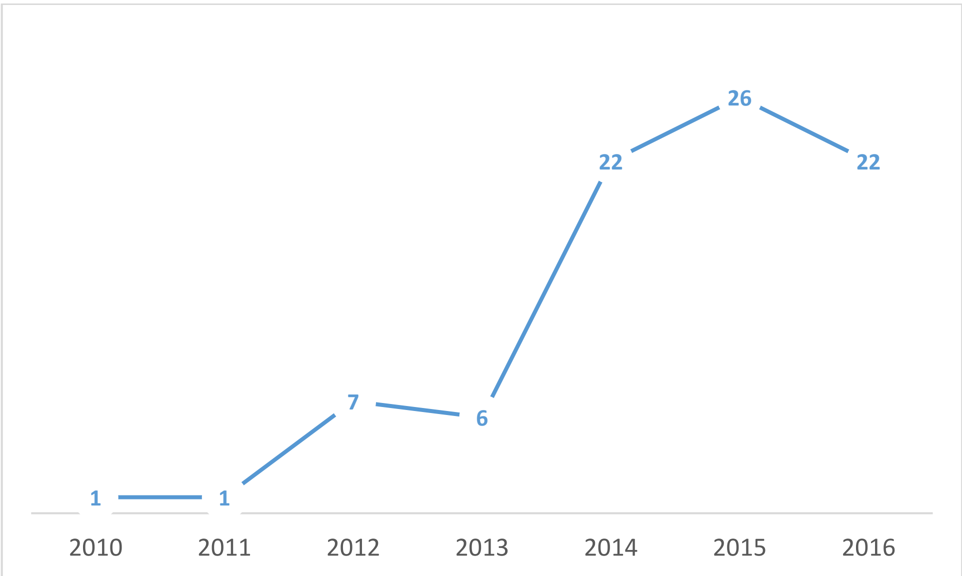

Figure 6. Trend of DLNM use by year

1.4. Goals and Objectives

As discussed in the previous chapter, there is a need to understand the risks regarding temperature and its relation to mortality in the Philippine setting. In connection to this, the main objective of this study is to primarily assess the relevant temperature-mortality associations in the Philippines.

By doing so, the following study-specific objectives were formulated to support and address the main objective of this manuscript:

1) **STUDY 1:** To determine the temperature-mortality relationship or the risk curve;
2) **STUDY 2:** To determine the effect modification by mortality subgroups;
3) **STUDY 3:** To disentangle the mean temperature effects from the heatwave effects; and,
4) **STUDY 4:** To determine the effects of the various temperature indices (mean temperature, inter- and intra-day variations) with respect to human health.

CHAPTER 2: STUDY 1 - Evaluating the Effects of Temperature on Mortality in Manila City, Philippines from 2006–2010 Using a Distributed Lag Nonlinear Model

The following studies were conducted to answer the research motivation of this PhD thesis; to profile the risks attributed to the temperature-mortality relationship in the Philippines. This portfolio of studies can and will contribute not just to the bigger body of knowledge, but also to the current and future policy directions addressing the effects of climate change on health.

In this study, we explored the plausibility of whether the prominent risks observed in temperate and other countries where the analyses have been carried out will hold through in the context of the Philippine setting. This is the first study to analyze the temperature-mortality relationship in Manila City, Philippines using daily data.

2.1. Methods

2.1.1. Climate and Mortality Data

We collected the meteorological variables such as daily average temperature, daily average humidity and daily average dewpoint with the study period of 2006-2010 from the Philippine Atmospheric Geophysical and Astronomical Services Administration (PAGASA). We obtained the same period of daily counts of deaths from the PSA-NSO which were coded with the *International Classification of Diseases (ICD) 10*. We categorized the mortality data by cause, sex, age, and season in order to observe the various levels of susceptibility. Cause-specific mortality for cardiovascular causes of deaths were determined through ICD codes I00-I99, while respiratory causes of deaths were J00-J99. Age-specific mortality was grouped into 0-14 y.o., 15-64 y.o., and >=65y.o.

We have coded the season-specific mortality based on PAGASA classification of seasons; namely, December-January-February (DJF) for the northeast monsoon season, March-April-May (MAM) for the summer season, June-July-August for the southwest monsoon season, and September-October-November (SON) for the transitional period from southwest to northeast monsoon season (Cinco et al. 2013).

2.1.2. Modeling Approach

We used Poisson generalized linear models with over-dispersion for the time-series data to evaluate the non-linear relationship of temperature and mortality (Gouveia et al. 2003; Ha et al. 2011a). In the initial analysis, the temperature-mortality relationship was analyzed using distributed lag non-linear model (DLNM) with natural cubic spline (NCS) as its smoothing parameter applied to both average temperature and lag dimensions; NCS-NCS model (Gasparrini et al. 2010; Ha et al. 2011a; Huynen et al. 2001; Ishigami et al. 2008). These splines relaxed the assumption of linearity for non-linear relationships which enables better fitting of the model. DLNM simultaneously analyzes the relationship of the non-linear pattern and the lagged effects which makes it an ideal tool for modeling temperature and mortality (Gasparrini and Armstrong 2013). Its flexibility in analysis enables the quantification of the lag effects while temperature and mortality are being modeled at the same time. We used different predictor space functions in this study while maintaining the lag space with NCS. There are also other predictor space functions which can be used, but these are discussed elsewhere (Gasparrini 2011).

In the initial diagnostics, we used an NCS-NCS model with the following parameterization:

$$Log[E(Y_t)] = \alpha + \beta T_{t,l} + ns(date, 7 * 5) + ns(RHave_t, 3) +$$

$$ns(dewpoint_t, 3) + as.factor(dow) + hod \quad [1]$$

Included within the initial model are variables such as the expected value of the daily counts of mortality (Y_t), which follows an overdispersed Poisson distribution, vector of regression coefficients for the crossbasis (β), crossbasis in pre-determined temperature and lag dimensions ($T_{t,l}$), seasonal variations (*date*), daily average relative humidity ($RHave_t$), daily average dewpoint ($dewpoint_t$), day of the week (*dow*), and holiday (*hod*). Based on previous studies, we have chosen 3 degrees of freedom (df) for $RHave_t$ and $dewpoint_t$, while 7df per year for *date* was used to control for the seasonal and long-term trends (Ishigami et al. 2008; Kaiser et al. 2002). *dow* is as a factor of indicator variables and *hod* being a binary variable. We used the city's annual population as an offset to control for changes in the population size through time.

In the df-selection for lag and temperature, we created a matrix of possible combinations which ranged from 4-15df for both lag and temperature dimensions with 1df increment. Akaike Information Criterion (AIC) was used as the basis for choosing the best df combination. We have observed that 7df for temperature and 4df for lag was considered to be the best combination which has the least AIC value. In the crossbasis function, both temperature and lag were set at equally-spaced knots based on the selected df in their dimensions; temperature percentile and log values of lag, respectively. Initially, we allowed the centering of the model into default, at the mean, to determine the MMT. After few model runs, we have determined that all-cause mortality MMT was at 30°C which was located exactly at the 80th temperature percentile. We used a 15-day maximum lag period to model the effects of temperature on mortality based on previous studies (Breitner et al. 2014; Ishigami et al. 2008).

In the NCS-NCS model, based on visual inspection as well as minimum mortality determination, we have observed that there are two minimum points at 25.8°C and 30°C. With increased susceptibility on both extreme tails resembling that of a U-shaped pattern we further analyzed it with a Double Threshold (DTHR) model set at the thresholds; a DTHR-NCS combination. We have altered Equation 1 and tailor-fit the thresholds into Equation 2 as seen below:

$$Log[E(Y_t)] = \alpha + \beta_{Low} TLow_{t,l} + \beta_{High} THigh_{t,l} + ns(date, 7*5) + ns(RHave_t, 3) + ns(dewpoint_t, 3) + as.factor(dow) + hod \quad [2]$$

The initial threshold values were based on the two minimum mortality points at 25.8°C for the low threshold and 30°C for the high threshold. β_{Low} and β_{High} serve as the vectors of regression coefficients for lower and higher temperature thresholds, respectively. In this study, we chose to refer to cold and heat effects as lower and higher temperature effects due to the subjectivity posed by the definition of cold and heat effects across the globe. In determining the best values for the DTHR-NCS analysis, we created combinations of multiple thresholds with 0.1°C increment for the new low threshold (lowest range value until 25.8°C) and the new high threshold (30°C until highest range value). Based on the AIC values of the multiple threshold combinations, the new low threshold was set at 23.6°C and the new high threshold was at 30.2°C. But given that the minimum temperature value in Manila City was at 23.5°C, the 0.1°C difference might not be able to capture the lower temperature effects and can be considered negligible, thus we further proceeded with a hockey-stick model with a Single High Threshold (STHR) at 30.2°C as the final model for temperature and all-cause mortality. $\beta_{High'}$ serves as the vector of regression coefficients of the new high threshold for the STHR-NCS model in Equation 3.

$$Log[E(Y_t)] = \alpha + \beta_{High'} THigh'_{t,l} + ns(date, 7 * 5) + ns(RHave_t, 3) + ns(dewpoint_t, 3) + as.factor(dow) + hod \quad [3]$$

For the category-specific mortality analyses, cause-specific, sex-specific, age-specific, and season-specific, we initially set them to the NCS-NCS specification, then objectively modified them based on their respective MMTs, knots, other model simplification procedures, as well as possible threshold points. Not all the models have a DTHR-NCS or STHR-NCS specification, but all have the same starting parameters in their NCS-NCS models, while season-specific analysis was treated differently in the study. According to Gasparrini (2011), the ordered series which are equally-spaced for the specific season in the respective years will not be able to constitute a single continuous series compared to the other analyses, thus this merits different parameterization as seen in Equation 4.

$$Log[E(Y'_{season})] = \alpha + \beta_{season} T_{season,l} + ns(doy_{season}, 4) + ns(time_{season}, 3) + ns(RHave_{season}, 3) + ns(dewpoint_{season}, 3) + as.factor(dow_{season}) + hod_{season} \quad [4]$$

We followed Gasparrini (2011) specifications in using the day of the year (doy_{season}) to control for the seasonal effect per year and time ($time_{season}$) to account for the long-term trend; the rest are season-specific parameters. We have observed extremely wide confidence intervals in the initial diagnostics which suppressed model pattern identification, thus we opted to use the log-transformed season-specific mortality (Y'_{season}).

2.2. Results

Table 1 shows the summary statistics of the meteorological and mortality variables of Manila City. There is a total of 94,656 all-cause deaths from 2006-2010 with cardiovascular causes of mortality making up 28.3% of all-cause mortality, while 12.4% was of respiratory causes of mortality. Larger proportion of sex-specific mortality is observed with males (57.1%) while females were at 42.9%. 51.1% constitutes the 15-64y.o. mortality, 32.1% of the >=65y.o. mortality and 16.8% for the 0-14y.o. The city experiences a narrow temperature range from 23.5°C to 33.3°C all year-round with the highest temperature recorded in MAM and lowest in DJF.

Table 1. Summary Statistics of Meteorological and Mortality variables in Manila City from 2006-2010

Statistic	Mean	S.D	Min	10th Percentile	50th Percentile	90th Percentile	Max
Average Temperature	28.8	1.52	23.5	26.8	28.8	30.7	33.3
Average Relative Humidity	73.9	7.46	53.0	64.0	74.0	83.0	100
Average Dewpoint	23.6	1.61	16.4	21.3	24.0	25.2	27.8
Season-specific Temperature							
DJF	27.6	1.19	23.5	26.1	27.6	29.0	30.5
MAM	29.8	1.36	24.8	28.2	29.8	31.5	33.3
JJA	29.1	1.37	24.8	27.3	29.2	30.8	32.5
SON	28.6	1.15	23.5	27.0	28.7	29.9	31.5
All-Cause Mortality	52.0	8.00	14.0	42.0	52.0	63.0	81.0
Cause-specific Mortality							
Cardiovascular	14.7	4.03	1.00	10.0	14.0	20.0	29.0
Respiratory	6.44	2.79	0.00	3.00	6.00	10.0	18.0
Sex-specific Mortality							
Female	22.3	5.24	3.00	16.0	22.0	29.0	38.0
Male	29.7	5.98	7.00	22.0	29.0	37.0	53.0
Age-specific Mortality							
0-14y.o.	8.70	3.23	0.00	5.00	9.00	13.0	21.0
15-64y.o.	26.5	5.68	6.00	20.0	26.0	34.0	48.0
>=65y.o.	16.7	4.31	2.00	11.0	16.0	22.0	31.0
Season-specific Mortality							
DJF	51.4	7.33	31.0	42.0	51.0	61.0	70.0
MAM	50.1	8.37	27.0	40.0	49.0	61.0	81.0
JJA	52.8	9.02	14.0	42.0	52.0	64.0	78.0
SON	53.3	8.53	15.0	43.0	53.0	64.0	75.0

Figures 7a-c show the model transition from the NCS-NCS, DTHR-NCS and STHR-NCS parameterizations of temperature and all-cause mortality. Figure 7a shows the NCS-NCS model with increasing risk in both tails with an MMT at 30.0°C located in the 80th temperature percentile. Figure 7b assumes a DTHR-NCS model with threshold points set at the minimum points observed in Figure 7a. Figure 7c shows a linear increase of temperature and all-cause mortality relationship with the new high threshold at 30.2°C.

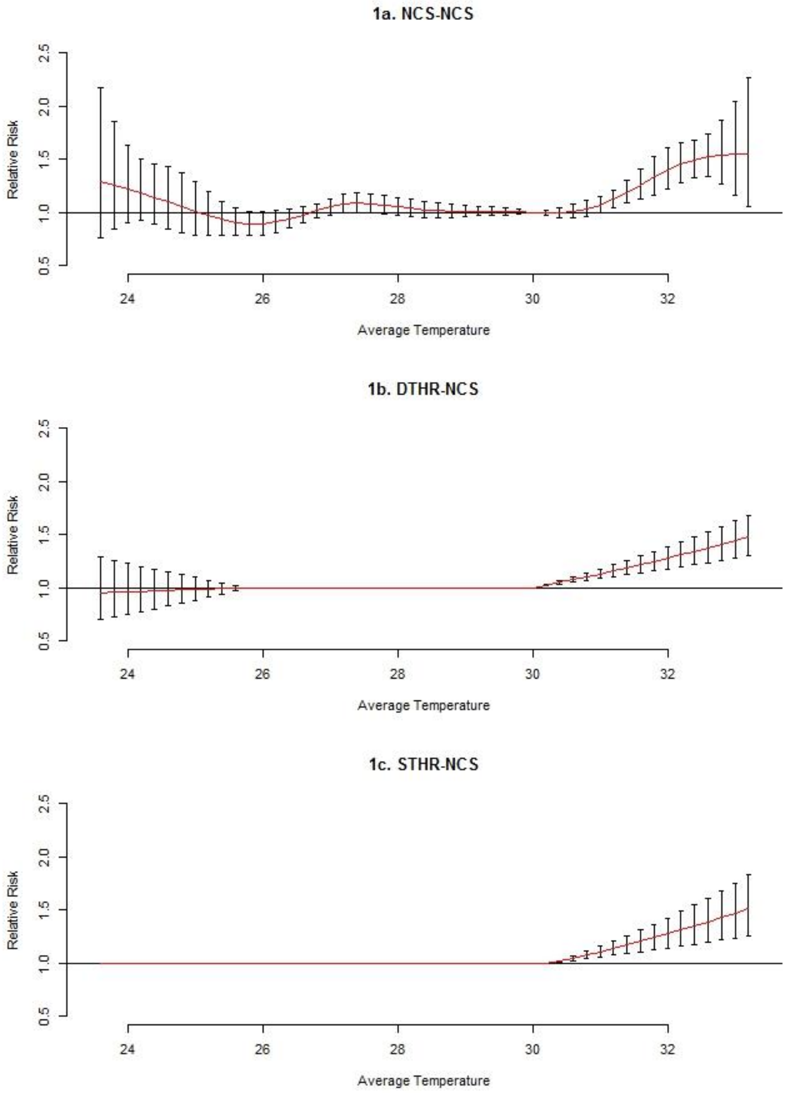

Figure 7. Model Parameterization with NCS-NCS (7a), DTHR-NCS (7b), and STHR-NCS (7c). DTHR-NCS thresholds were set at the two minimum points observed in NCS-NCS, while the upper threshold in STHR-NCS was based on the best combination of the upper and lower threshold resulting to negligible lower temperature effects.

In Figures 8 and 9, located at the right side are the simplified models we have derived which can also reflect the relationship as good as or better than the NCS-NCS model on the left side except for the male mortality where NCS-NCS outperforms the STHR-NCS. In the cause-specific analysis, Figures 8a-d show that there are higher risks for respiratory causes of mortality compared to those with circulatory-caused mortality in higher temperatures. We have also observed a difference between the susceptibility with high temperature among males and females seen in Figures 8e-h, whereby females have higher risks than males.

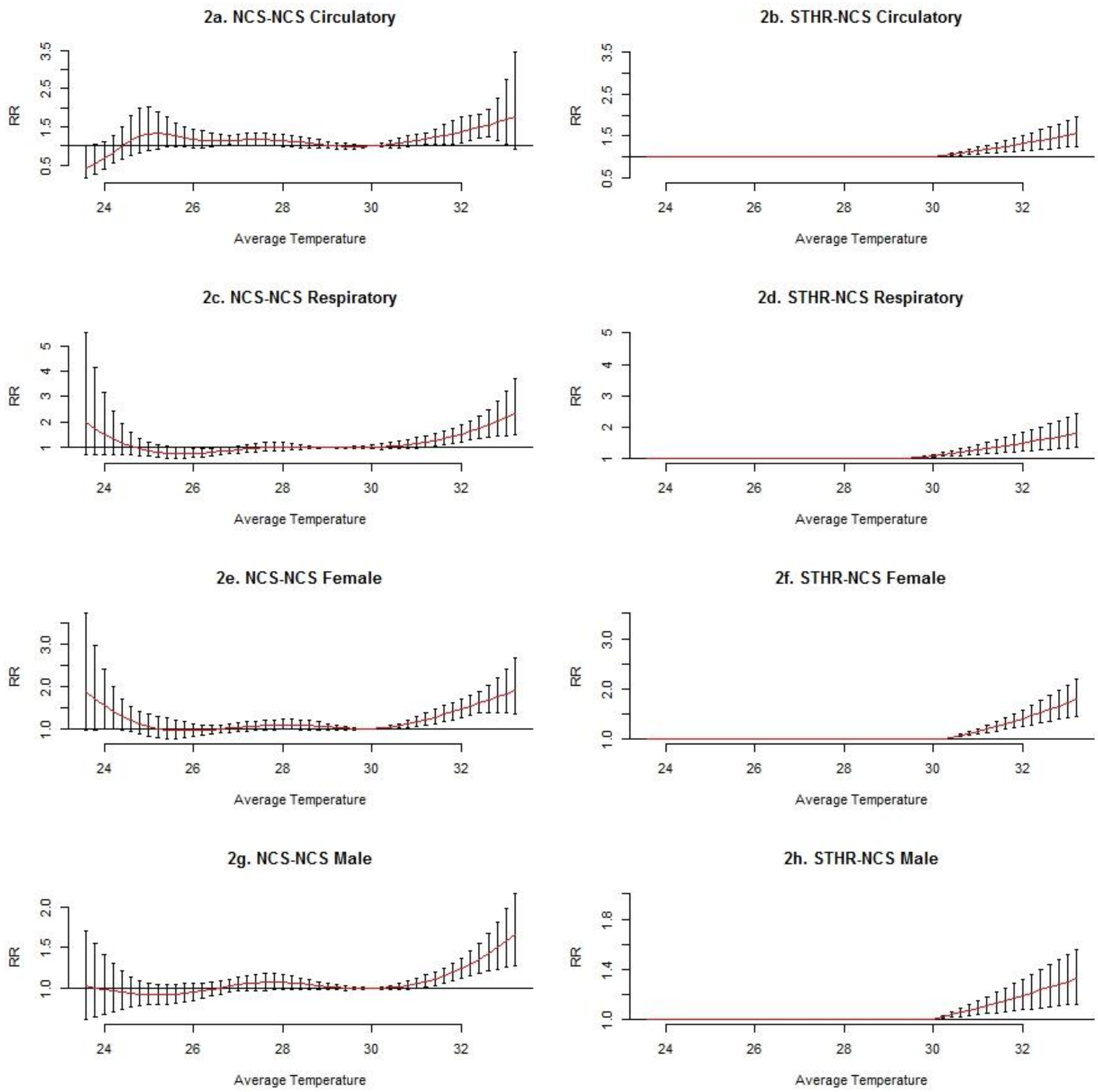

Figure 8. Cause-specific (8a-d) and Sex-specific mortality (8e-h) RR in both NCS-NCS and STHR-NCS models. Upper thresholds in the STHR-NCS models were based on the respective observed minimum mortality points.

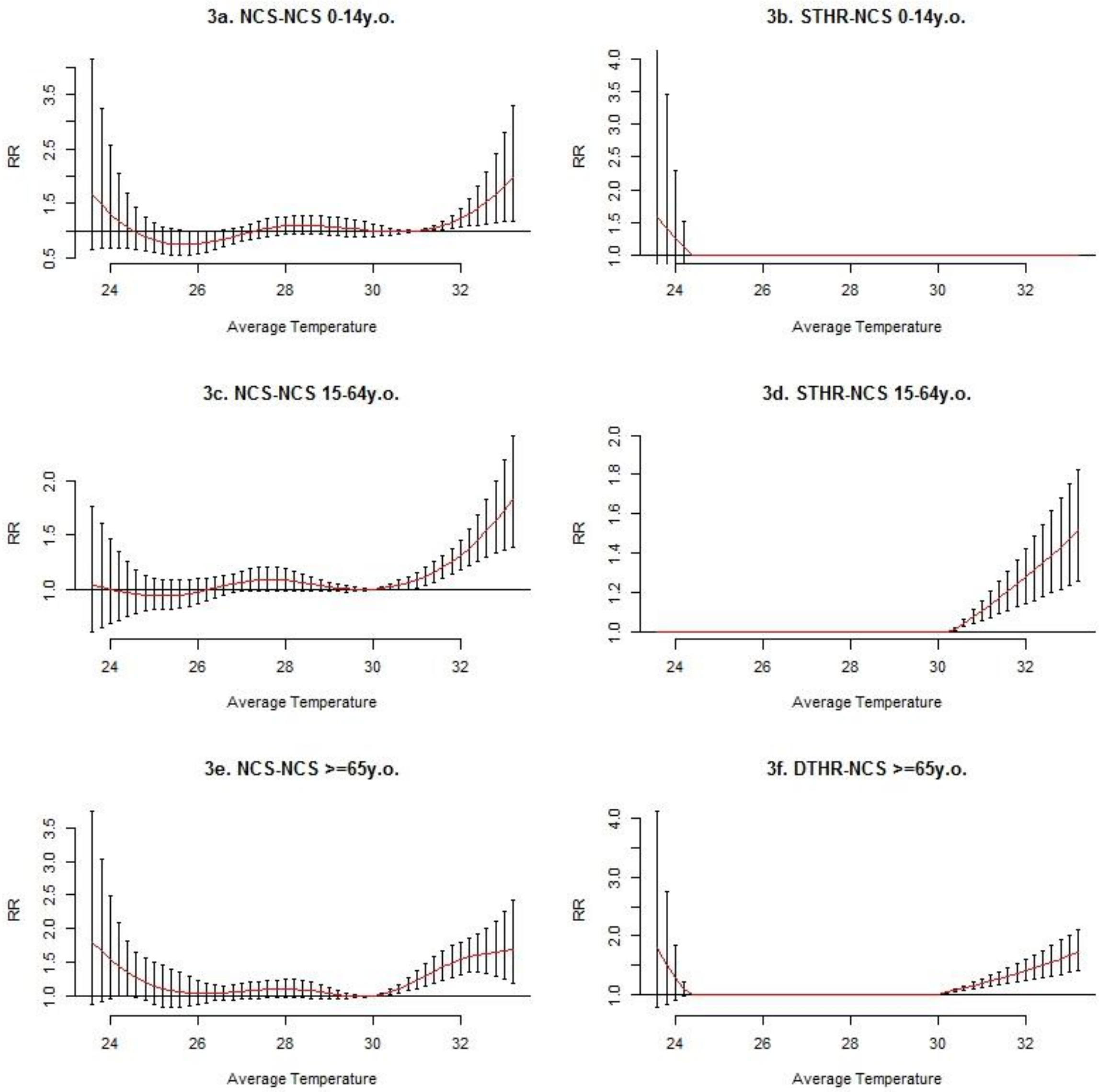

Figure 9**.** Age-related RR in NCS-NCS, DTHR-NCS and STHR-NCS models. Only the >=65 y.o. (*9e-f*) resulted to a DTHR-NCS because of its prominent lower temperature effects and higher temperature; all other age groups were reduced to STHR-NCS as their final form with 0-14y.o. (*9b*) having pronounced lower temperature effects.

Among the age-specific mortality in Figure 9, >=65y.o. age group experiences a higher risk compared to the other two age groups. This pattern is also evident in other studies taking into consideration the vulnerability of the age groups towards physiological capacity to heat tolerance. The 15-64y.o. age group (Figure 9d) exhibits higher temperature effects, while 0-14y.o. age group in Figure 9b shows pronounced lower temperature effects.

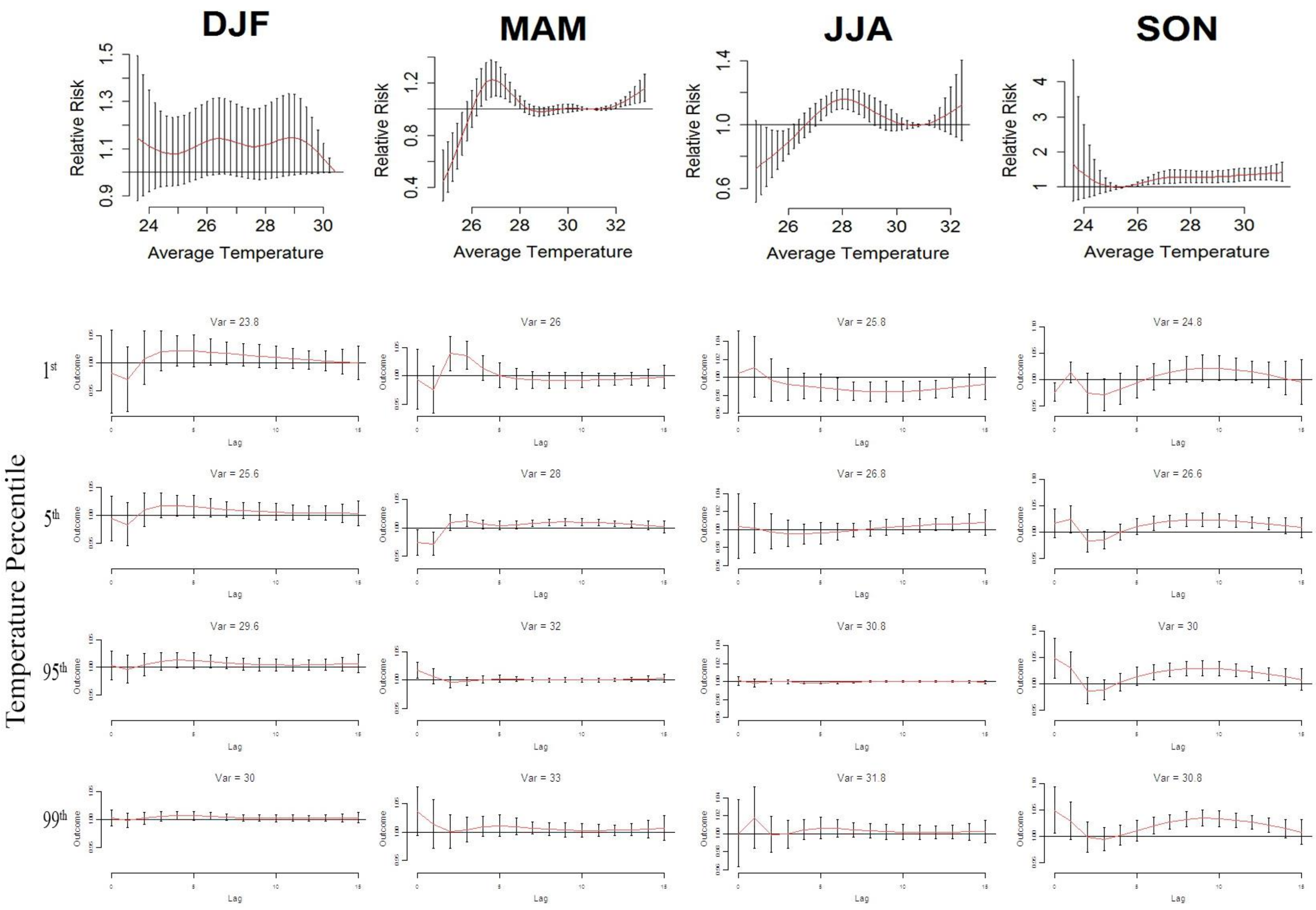

Figure 10. Season-specific RR with temperature-specific risks. Season-specific all-cause mortality and average temperature relationships are located in the upper most part followed by the temperature slices in their respective temperature scales; 1st, 5th, 95th, and 99th percentile, respectively.

Figure 10 shows the increased risk in MAM and SON in the higher temperature percentile. A possible "harvesting"/mortality displacement can be observed in SON's temperature-specific risks but this was not yet ascertained as this is beyond the scope of the study. This seasonal confounding is supported by Figure 11 showing the monthly distribution of rainfall by year in Manila City which can bring about increased cases of water-borne diseases thereby affecting risks (PSA-PhilSIS 2014). Increased amount of rainfall can be observed in JJA with gradual decline towards entering SON.

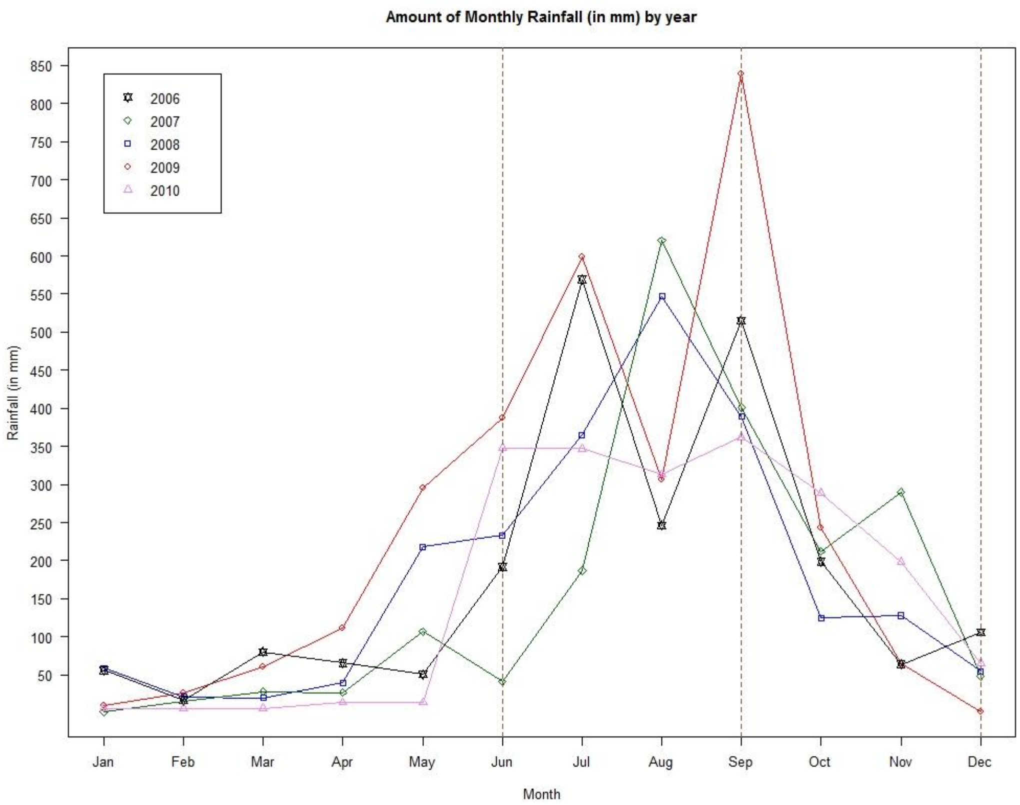

Figure 11. Amount of Monthly Rainfall (in mm) by year in Manila City. The reference lines indicate the periods of JJA and SON seasons. Increased amount of rainfall can be observed in JJA with decreasing pattern as it continues to SON.

2.3. Discussion

In this study, we have identified that the effects of temperature on mortality conforms with the non-linear patterns observed in the previous studies of temperate and sub-tropical cities (Chung et al. 2009; Curriero et al. 2002; El-Zein et al. 2004; Guo et al. 2013; Ha et al. 2011a; Ha et al. 2011b; Huynen et al. 2001; Ishigami et al. 2008; Lin et al. 2011; Motohashi et al. 1996; Plavcova and Kysely 2010). The temperature-mortality relationship was seen to have a U-shaped pattern with elevated risks in both lower temperature and higher temperature slopes and an observed prominent increase towards the higher temperature end. The existence of two points in the model warranted the use of a DTHR-NCS. DTHR-NCS allows us to assume linearity beyond the threshold points and a null relationship in between the points (Gasparrini 2011). The tradeoff of using a STHR-NCS or DTHR-NCS instead of an NCS-NCS parameter in this study comes at the expense of having a restricted pattern, unlike that of the smoothed pattern, but with greater robustness when it comes to the specific sub-models in the analyses.

When we conducted a sensitivity analyses for the threshold selection in all-cause mortality, the new low threshold was not wide enough to capture the lower temperature effects, thus we only used the new high threshold for the STHR-NCS; compared to DTHR-NCS, STHR-NCS is more robust which explains 80.9% of the variability. STHR-NCS, aside from its robustness, also provides an ease of interpretation when it comes to policy considerations since the field of environmental epidemiology, especially in the context of temperature and mortality is still a developing discipline in the country. It is worthy to note that as the model parameterization changes in the temperature and all-cause mortality relationship, there is still consistent high temperature effects with relatively same risks.

To further quantify the effects of temperature on mortality, we have classified the analyses into cause-specific, sex-specific, age-specific, and season-specific analyses. In most of the models, higher risks are observed in the higher temperature slope of the relationship which is consistent with the results of other studies (Chung et al. 2009; Curriero et al. 2002; Guo et al. 2013; Ha et al. 2011b; Ishigami et al. 2008; Lin et al. 2011; Motohashi et al. 1996; Plavcova and Kysely 2010). Hereafter, we refer to the RR in the 99th temperature percentile of the NCS-NCS model to standardize the interpretation of RR across the models. In the cause-specific analyses, we have observed a greater risk for respiratory causes of mortality (RR=1.52, 95% CI: 1.23-1.88) more than that of the cardiovascular causes (RR=1.37, 95% CI: 1.07-1.75). This result is consistent with those observed by Ballester et al. (1997) and D'Ippoliti et al. (2010), wherein hot air can deter respiratory functions for those suffering with chronic respiratory diseases in high temperature periods.

Sex-specific analyses showed that females (RR=1.47, 95% CI: 1.27-1.69) have higher risks compared to males (RR=1.24, 95% CI: 1.13-1.37) which is similar with other studies (D'Ippoliti et al. 2010; Son et al. 2012; Xiang et al. 2014). However, studies by Basu and Ostro (2008) and Huang et al. (2010) have shown that there is no significant difference between the two groups. The difference observed in the study between the sexes can be attributed to their respective physiological orientation and can be also affected by effect modifiers in the area (Ma et al. 2015; Zeng et al. 2014). A study by Kazman et al. (2015) has showed that VO_2max, the maximal oxygen uptake test to assess aerobic power, played a big role in the heat tolerance between the sexes. Lower VO_2max was found to be associated with maximum heart rate and physiological strain even after controlling for sex. VO_2max is deterrent in conditions where heat loss is strongly limited by high temperature and humidity (Havenith 2005).

The elderly population aged >=65y.o. has the highest RR at 1.53 (95% CI: 1.31-1.78). As the human body age, the thermoregulative capacity to adapt to heat stress is impaired increasing the risk to those who already have pre-existing health problems (Basu and Ostro 2008; D'Ippoliti et al. 2010; Michelozzi et al. 2009; Son et al. 2012). We have observed that 0-14y.o. age group has greater susceptibility towards the lower temperature effects as shown in Figure 9b similar to those observed by Gouveia (2003); however, the wide confidence interval indicates possible confounding by unaccounted variables, such as diarrhea (Carlton et al. 2014).

In the season-specific analyses, we used the log-transformed season-specific mortality to adjust for the very wide confidence intervals seen in the initial diagnostics. We have observed that MAM, the summer season, records the highest temperature at 33.3°C for five years in Manila City which is evident in the higher temperature slope having high relative risk (RR=1.13, 95% CI:1.05-1.22). Most people go out during summer time especially to beaches or simply while traveling which increases the exposure to the heat of the sun. We have also noted that SON, at Lag 0, has a wider low temperature effects. But it remains inconclusive with regard to its lower temperature effects as the confidence interval is rather wide which can be caused by the potential confounders such as diarrhea and leptospirosis brought about by above-average rainfall (Hales et al. 2014; Wilkinson 2014). Chadsuthi et al. (2012) and Carlton et al. (2014) have noted that rainfall increases the susceptibility towards diarrhea and leptospirosis. Due to daily data unavailability, we were not able to explore the possibility of confounding of diarrhea or leptospirosis in the temperature-mortality relationship. However, it is worthy to note that in one of the National Epidemiology Center's (NEC) reports, leptospirosis was observed to peak somewhere in SON while acute bloody diarrhea gradually increases from JJA until SON before subsiding in DJF (NEC 2009). Though the pattern may be promising, the national report has a loophole of either overestimating or underestimating the effects of diarrhea or leptospirosis in Manila City as the report captures the overall nationwide cases and is also limited to a specific timeframe. We have also noted a possible harvesting in SON based on its 5th and 95th temperature percentiles in Figure 10. The rainy season of JJA, with the highest amounts of rainfall in Figure 11, might have posed initial risks for those with chronic illnesses and which were carried over to SON which resulted to death; chronic diseases take time to manifest, especially the respiratory-related ones. These possibilities remain unexplored due to the unavailability of daily rainfall data and other parameters which can affect harvesting or explain the wide confidence interval observed in SON and in season-specific analysis.

This is the first study which conducts a DLNM analysis in determining the temperature-mortality relationship in the Philippines, specifically in Manila City. In this study, we have analyzed comprehensively the risks attributed to cause, sex, age, and season. Our findings can be used for early warning measures for city-specific responses in Manila City, such as those already installed heat-health warning systems in Australia (Queensland), Belarus, Italy, Spain, UK, US and more (WMO-WHO 2015). In Philadelphia, a Hot Weather-Health Watch/Warning System was initiated in 1995 to alert the city's population of the incoming risks brought upon by extreme weather events (Ebi et al. 2004). Ebi et al. (2004) found out that issuing an individual warning lowered daily mortality by about 2.6 lives on average in Philadelphia. Similar findings were observed in Adelaide, Australia, whereby marked reductions in renal and heat-related morbidity in 2014 were recorded, after installing the heat warning system (HWS) in 2009 (Nitschke et al. 2016). These previous studies have shown the importance of an HWS, and the only way to achieve this is through an evidence-based approach. For further readings of HWS, we invite the readers to read a joint report by WMO-WHO (2015), whereby they have exclusively devoted a chapter for the said topic, and have listed almost 23 countries with existing HWS; in Chapter 4, Table 4.

It should be noted that the results of the study might not hold through with the implications in the different areas in the Philippines, as these cities or municipalities have different temperature ranges, mortality rates and other area-specific parameters, which can affect both the risks and the unaccounted underlying mechanisms. The study is limited to the use of available meteorological factors and did not consider the use of daily air pollutant concentrations in Manila City due to data unavailability. Real-time PM measurement has just started in the country and the available data does not coincide with the gathered mortality and meteorological dataset time window. There is a need to also explore the effects of air pollution in the temperature-mortality pattern as pollutant concentration also affects the relationship (Guo et al. 2014b). Further research are warranted in verifying harvesting and as well the impact of possible confounders, such as diarrhea and leptospirosis, into the season-specific analysis.

CHAPTER 3: STUDY 2 - Effect Modification in the temperature extremes by mortality subgroups among the tropical cities of the Philippines

The first study has established the risk curves with respect to the temperature-mortality relationship of Manila city which was able to note of the following observations: 1) some effects estimate to be increased in certain risk population, and 2) prominent effects were prominent in the extreme temperatures. The aforementioned observations inspired the second study, which focused on the effect modification brought about by the mortality subgroups in the three metropolitan cities in the Philippines. In stricter sense, all-cause mortality subgroups are the groupings whereby all-cause mortality can be classified into, all throughout the paper we will refer to the usage of mortality subgroup as synonymous to all-cause mortality subgroups.

Various studies have noted the effect modification brought about by different subgroups (Ding et al. 2016; Medina-Ramon et al. 2006b; O'Neill 2003; O'Neill et al. 2003). Basu (2009) extensively reviewed multiple studies which noted that risks vary, particularly by cause of death, sex, age and even season. For further reading, please refer to Basu (2009) Table 3, wherein she laid out a summary table of the different studies of temperature and mortality and the subgroups experiencing the elevated risks.

3.1. Methods

The study sites are located in the three metropolitan cities in Philippines, as seen in Figure 12. These three big clusters house the three metropolitan cities of the country, which serve as the centers of business and commerce in the respective cluster.

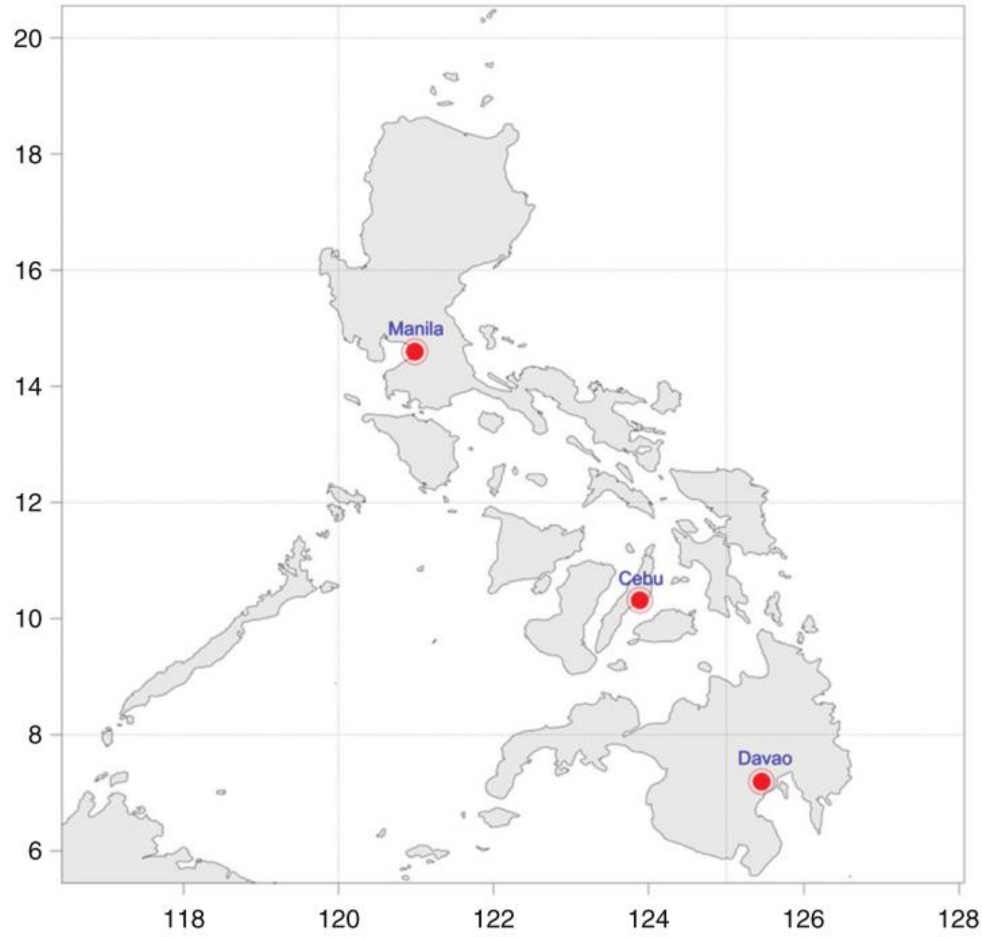

Figure 12. Geographical Location of the three Metropolitan Cities of the Philippines

3.1.1. Meteorological and Mortality Data

We collected both the 2006-2010 daily average meteorological and daily mortality variables from the PAGASA and Philippine Statistics Authority – National Statistics Office (PSA-NSO), respectively. Mortality data was then divided according to cause of death, sex, and age. We used the ICD 10 codes to segregate cardiovascular-related deaths (I00-I99) and respiratory-related deaths (J00-J99) from the all-cause mortality counts, while we created three groups for age-specific mortality, namely: 0-14 years old, 15-64 years old, and >64 years old. We set the extreme low temperatures at the 1^{st} and 5^{th} temperature percentiles, and the extreme high temperatures at the 95^{th} and 99^{th} temperature percentiles.

3.1.2. Statistical Analyses

We performed a two-stage analysis to estimate the extreme temperature effects stratified by mortality subgroups to observe the effect modification. In the first stage analysis, we analyzed the temperature-mortality relationship using a time series analysis with Poisson distribution, accounting for over-dispersion, subjected to a distributed lag non-linear model (DLNM) parameterization, as seen below (Armstrong and Gasparrini 2012; Gasparrini et al. 2010; Gasparrini 2011):

$$\log(\mu_t^c) = \alpha + \beta T_{t,l} + ns(date, 7 \times 5) + ns(RHave_t, 3) + as.factor(dow) + \varepsilon_t \quad [1]$$

where $\log(\mu_t^c)$ is the expected value of the log of mortality on city (c) and time (t); α is the intercept; β as vector of regression coefficients for the crossbasis ($T_{t,l}$) in pre-determined temperature and lag dimensions; ns is the smoothing parameter set to natural cubic spline; $date$ controls for seasonal variations with a total of 35 degrees of freedom (df); $RHave_t$ is the relative humidity as a covariate on time (t) with 3df. dow is day of the week as a factor of categorical variables; ε_t is the residual. The selection of df for the covariates are based on previous studies (Gasparrini 2011; Guo et al. 2011). In the model fitting process, we used the natural cubic spline (NCS)-NCS specification in the cross-basis function of DLNM (Seposo et al. 2015). By using the Quasi-Poisson Akaike Information Criterion (QAIC) for model parameterization (Gasparrini 2014), we were able to determine that the combination of 4 df for both temperature and lag dimensions, respectively, was considered to be the best fit having the least QAIC value.

In the second stage analysis, we pooled the city-specific estimates using a random-effects meta-analysis:

$$\log(\mu_t^{c*}) = \hat{\beta} + \delta_c + \varepsilon_c \qquad [2]$$

where $\log(\mu_t^{c*})$is the effects estimate of city (c) in the first stage analysis, $\hat{\beta}$ is the pooled estimate to be determined with δ_c as a vector of within-city random effects by city (c), and ε_c represents the between-cities random errors (Jhun et al. 2014; Nordio et al. 2015). City-specific estimates in the second stage analysis were assumed to be normally distributed. After pooling the city-specific estimates, we stratified the pooled pattern by cause of death, sex, and age to determine the effects estimates due to effect modification.

All analyses were carried using R programming through the following packages: "*ggmap*" and "*maps*" for geographical location determination, "*dlnm*" for city-specific estimates estimation, and "*mvmeta*" for meta-analysis.

3.2. Results

Table 2 shows the descriptive statistics of both meteorological and mortality data from the three cities in 2006-2010 with a total of 182,908 mortality counts and an average temperature well within the range at 28°C. Among the cities, 50% of the mortality counts were from Manila (n=94,656), with the other half from both Cebu and Davao. In order to observe the effect modification, we stratified by mortality subgroups namely, cause of death, sex, and age.

Table 2. Descriptive Statistics of the meteorological and mortality statistics per city (N=182,908)

Variables (Mean±S.D.)	Manila (n=94,656)	Cebu (n=43,830)	Davao (n=44,422)
Average temperature (°C)	28.8±1.52	28.2±1.16	28.1±1.00
Average relative humidity (%)	73.9±7.46	82.5±5.43	82.1±4.35
All-cause mortality	52±8	24±5	24±5
Cause-specific mortality			
Cardiovascular	15±4	7±3	9±3
Respiratory	6±3	3±2	2±2
Sex-specific mortality			
Women	22±5	10±5	10±3
Men	30±6	14±6	15±4
Age-specific mortality			
0-14 years old	9±3	3±2	2±1
15-64 years old	27±6	12±9	13±4
>64 years old	17±4	9±3	10±3

Figure 13 shows the 3-dimensional relationship of average temperature and RR on the various lags. All three cities have common immediate high temperature effects in lags 0-

2, with heightened risks observed in the lower temperature percentiles as shown in Figure S1. The effect estimates derived from the city-specific analysis through DLNM, were then pooled via meta-analytical techniques as mentioned in the previous section and are shown in Figure 14.

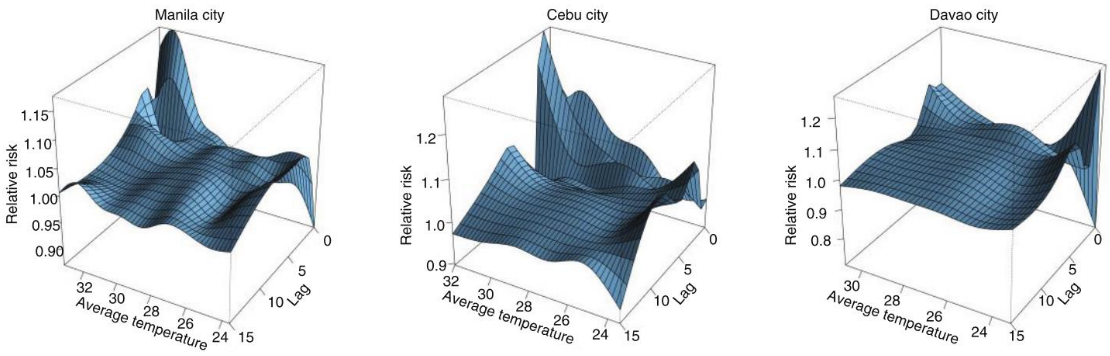

Figure 13. Distributed lag non-linear relationship of average temperature, lag and RR in the three cities from 2006-2010

The red line, pooled estimate, which passes through the dotted lines, city-specific estimates, attempts to create a suitable fit with respect to the city-specific information/estimates. Since there is no monotonous rise in the RR, we used the second local minimum as a reference temperature, which, in this case, is also the MMT located at the 70th temperature percentile marked with a vertical blue line.

The observed similarity in the all-cause mortality trend of the exposure-response relationship graphs among the three cities shown in Figure S2, resulted to a homogeneous pattern with an I-squared statistic equal to 1%. Evident high temperature effects were observed in the pooled relationship at the 99th temperature percentile (RR=2.48 CI: 1.55

– 3.98) and an elevate risk in the 1st temperature percentile (RR=1.23 CI: 0.88-1.72).

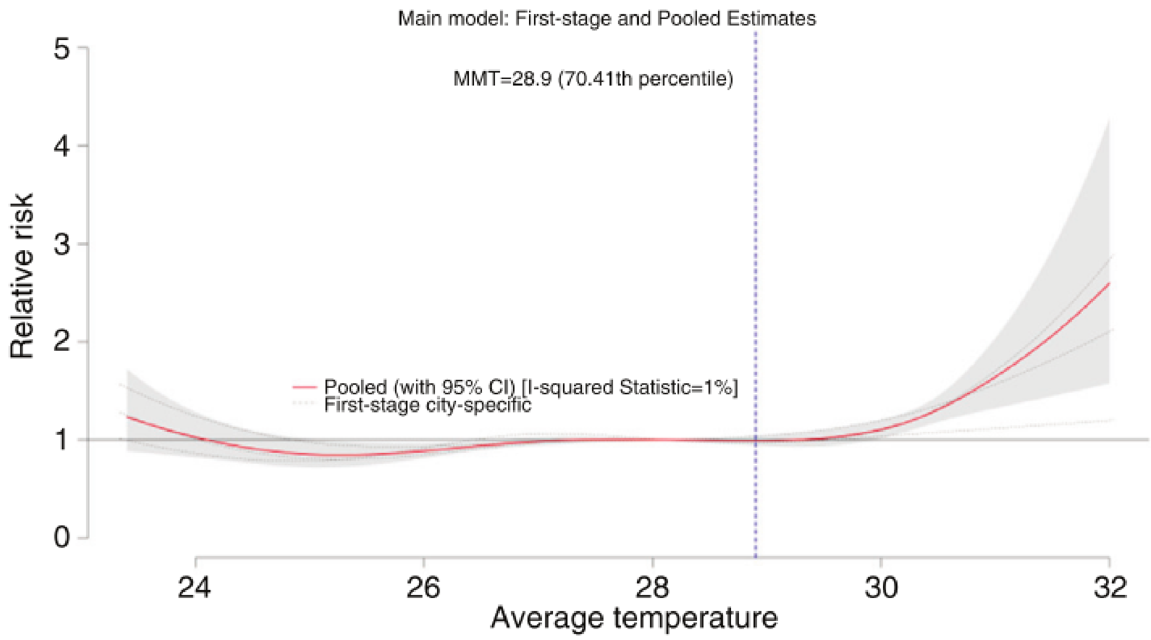

Figure 14. Meta-analysis of the pooled effects estimates from the three cities. The vertical blue marker serves as the point of MMT. The red line is the pooled estimate, while the dotted lines are the city-specific estimates (of the first stage analysis).

In Figure 15, lower temperature effects were observed to be higher in Cebu and Davao, while Manila has higher risks in the higher temperature. For city-specific analysis, we used the relative scales, which may prove to have more relevant implications to city-specific attributes compared to using absolute scales (Anderson and Bell 2009a). However, all-cause mortality might not truly reflect the trends by the subgroups, thus, inherent effect modification can be observed, as seen in Figure 16.

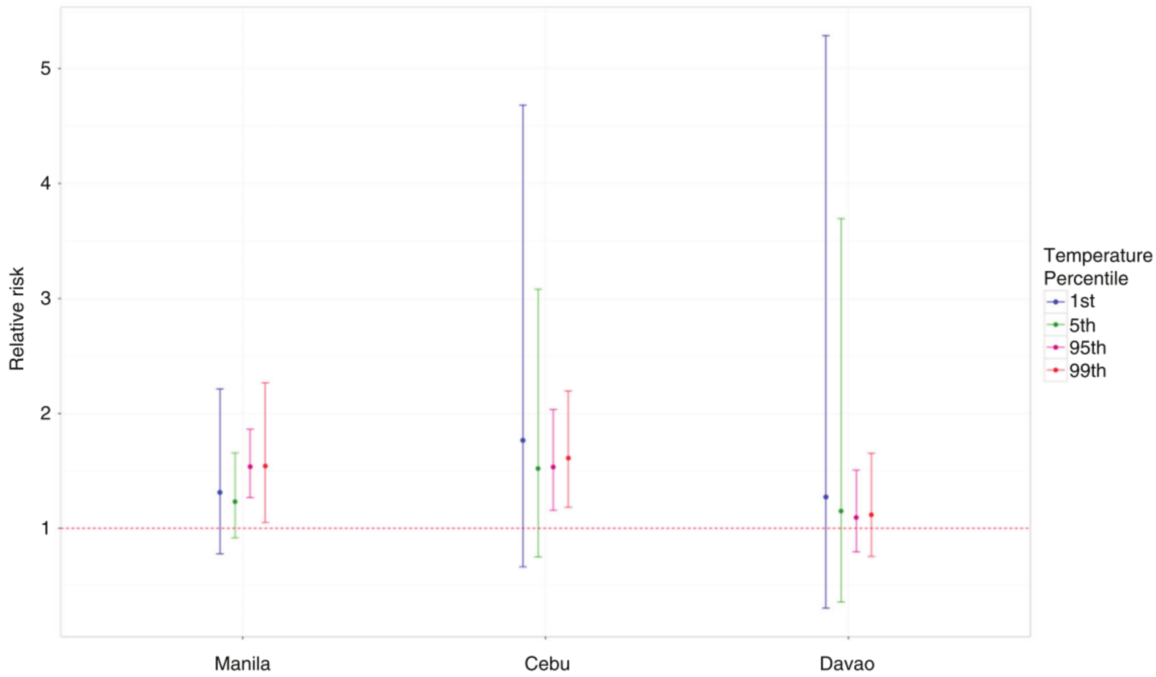

Figure 15. All-cause mortality per city on relative scale at the 1st, 5th, 95th and 99th temperature percentiles, respectively.

We opted to log-transform the RRs in Figure 16 since the non-transformed RRs had wide confidence intervals, which masked the other lower RRs. Among the mortality subgroups, we have observed variations in the causes of mortality in Figure S3.

In summary, the results have shown that at the aggregate level, using all-cause mortality, all the cities were found to be homogeneous. However, when disaggregated into the mortality subgroups, effect modification by cause of death, sex, and age were evident.

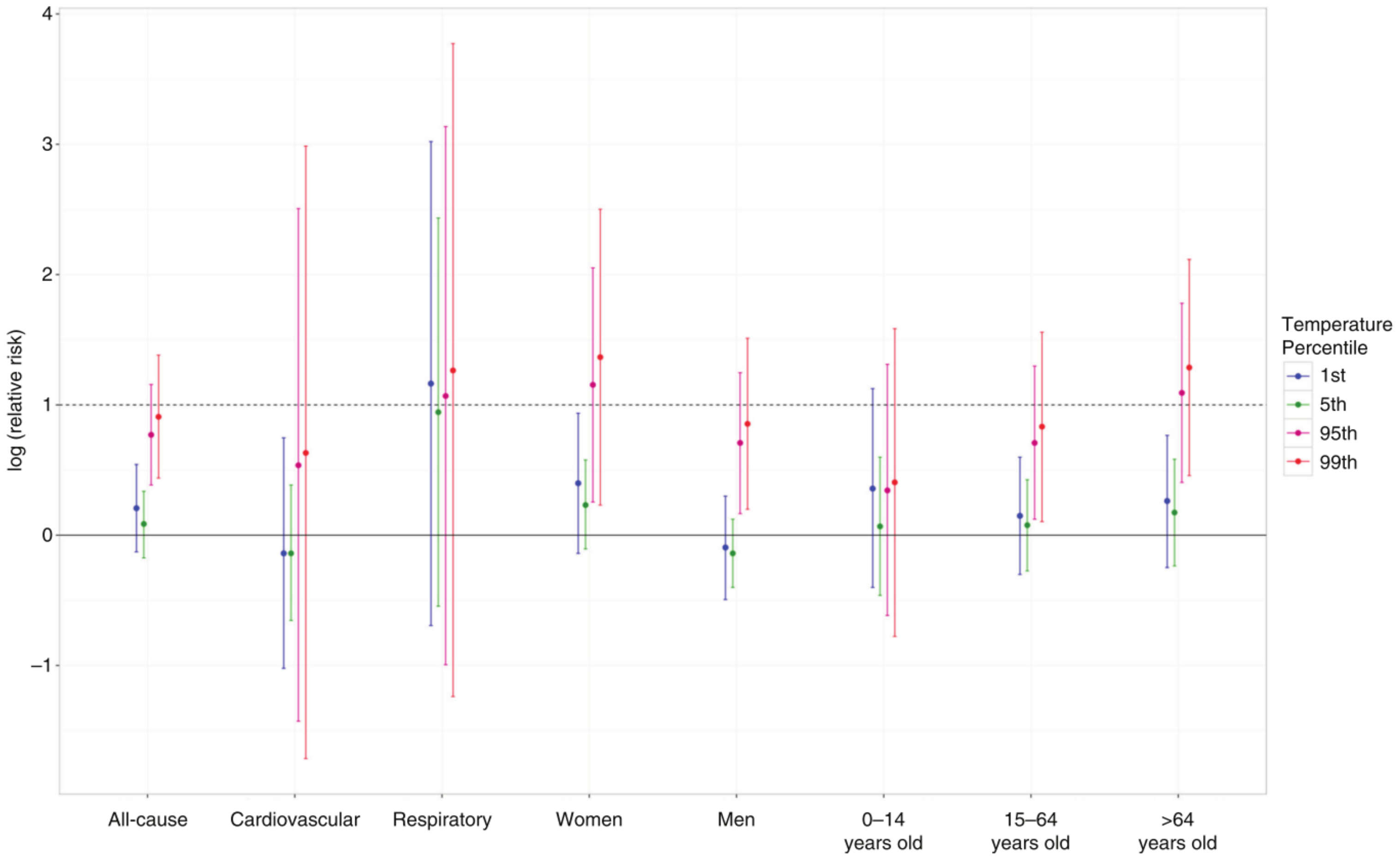

Figure 16. Log-transformed RRs showing the effect modification in the pooled pattern by various mortality subgroups at the 1^{st}, 5^{th}, 95^{th} and 99^{th} temperature percentiles, respectively. The dotted line marks the log of RR at 1.

3.3. Discussion

In this present study, we explored the effect modification brought about by the different mortality subgroups in the extreme temperatures among the three cities in the Philippines. The main findings of the study are that: 1) extreme high temperatures have greater risks compared to the different temperature percentiles; 2) higher risks were particularly observed in respiratory-related cases, women, and >64 years old; and 3) city-level variations in the risks can be linked to area-specific attributes.

The results of the study indicating that extreme high temperatures pose greater risks compared to the other parts of the temperature percentile are consistent with previous studies (McMichael et al. 2008; Medina-Ramon et al. 2006a; Medina-Ramon and Schwartz 2007b). A J-shaped pattern signifying an increased risk in the extreme high temperature is evident in the pooled pattern in Figure 14, and can be clearly deciphered through the stratification by mortality subgroups in Figure 16. Anderson and Bell (Anderson and Bell 2009a) and other similar observations from other studies (Breitner et al. 2014; Guo et al. 2014a) have shown that heat-related mortality, specifically in the extreme high temperature, is usually associated with shorter lags; which were observed to last from lags 0-2 (as seen Figure S1). Nevertheless, extreme low temperature effects were also observed in Figure S4 per city and per mortality subgroup, which lasts longer (at lag 5) than the extreme high temperature effects as shown in Figure S1. Extreme low temperature effects are typically observed in longer lags, as also noted in previous studies (Anderson and Bell 2009b; Breitner et al. 2014; Guo et al. 2011). Similar observations were observed with our study, whereby the extreme low temperature effects were delayed up to lag 5 and lasted until lag 15, Davao's case (as seen in Figure S1). In a multi-city, multi-country, similar observations of delayed and prolonged risks were observed in the extreme low temperature percentiles (Guo et al. 2014a).

More importantly, this study explored the effect modification brought about by cause of death, sex and age in both pooled and city-specific extreme temperature percentiles; the 1^{st} and 5^{th} being the extreme low temperature, and the 95^{th} and 99^{th} being the extreme high temperature. In Figure 16, extreme high temperature effects are prominent in individuals who have respiratory-related problems, females and >64 years old.

Respiratory causes of mortality having greater risk especially in the high temperatures is supported by previous studies, which indicated that hot temperature can be deleterious to people with chronic respiratory diseases (D'Ippoliti et al. 2010). Michelozzi, *et al. (2009)* points out the possibility of exacerbations of chronic obstructive pulmonary disease (COPD) in the hospital setting, and which were likely due to problems with excess heat dissipation through circulatory adjustment (Liu et al. 2011). On that same note, Michelozzi, *et al. (2009)* stressed that extreme temperatures increase the risk of those with COPD in developing pulmonary vascular resistance secondary to peripheral pooling of blood or hypovolemia.

With regard to women and men, both sexes have similar risk patterns with respect to extreme high temperatures having greater risks compared to extreme low temperatures. However, between the two, women have greater risks, in either extreme temperatures, compared to men, which is in concurrence with the results of previous studies (Basu 2009; Bell et al. 2008; D'Ippoliti et al. 2010; Son et al. 2012). On the other hand, some studies either showed that men have greater risks (Bell et al. 2008), or no difference at all (Basu and Ostro 2008; O'Neill et al. 2003). Though some researchers have reported that the difference between the two may be attributed to socio-economic factors and of geographical context (Hajat et al. 2005; O'Neill et al. 2003), the underlying factors and mechanisms resulting to these varying results across different areas warrant further investigation.

Results from the age-stratified analysis showed that the elderly, >64 years old, were experiencing the greatest risks in the extreme high temperature. This is consistent with previous studies, which indicate that the thermoregulatory capacity of a person deteriorates as the body ages (D'Ippoliti et al. 2010; Michelozzi et al. 2009; Stafoggia et al. 2009). Other socio-economic factors as well as social isolation can also affect the susceptibility of the elderly population (D'Ippoliti et al. 2010). Harlan et al. (2013) notes that socially-isolated elderly tend to have increased vulnerability to temperature effects.

However, we were not able to explore this possibility due to the lack of individual socio-economic parameters. The study's results with regard to the susceptibility with the various subgroups have similarities with those observed by *D'Ippoliti et al. (2010)* and Yang et al. (2012), whereby both studies have found that older females who suffer from respiratory-related diseases have greater risks. In Figure S3, pooled patterns of each individual characteristic across three cities were observed to have variations, most especially in the patterns of cardiovascular and respiratory causes of mortality. However, due to the limited number of cities, we were not able to carry out a meta-regression with area-specific meta-predictors, as there is little or no variations among the three cities, as seen in Figure 14.

The study is limited to the following: (1) number of cities, and (2) lack of air pollution data. Although there is no gold standard with respect to the number of cities to be included in the study, the inclusion of more cities may increase the statistical power of the analysis, likewise, will enable clearer detection of variations with respect to the explanatory variables. Also, we were unable to acquire the daily air pollution data for the said period, as the Philippines is currently institutionalizing the detection of particulate matter monitoring in the country.

The study has shown that greater risks were likely to be observed in the extreme temperatures. Furthermore, effect modification by mortality subgroups can be observed, especially with respiratory-related diseases, women, and elderly. Variations were observed in the causes of mortality, however, definite patterns are yet to be ascertained due to the limited number of cities included in the study. Generalizations of this study towards other tropical cities, or even within the Philippines should be taken into caution since the city-specific variables may vary from one area to the other.

CHAPTER 4: STUDY 3 - Exploring the Effects of High Temperature On Mortality in 4 Cities in the Philippines Using Various Heat Wave Definitions

The first two studies established the following: 1) risks are higher in the extreme temperatures, and 2) risks in the extreme temperature are effect modified by the mortality subgroup. In dealing with the temperature-mortality risk determination, there are instances whereby prolonged hot days, known as heatwaves (HW), may intensify the risks. However, only a limited number of studies have taken into consideration the HW component, even more, only few studies tried to separate the mean temperature effects (mean temperature effects) from the HW effects. Taking into account the results of the first two studies, the third study aimed to disentangle the HW effects, based on different HW definitions, from the mean temperature effects.

4.1. Methods

Mortality data and meteorological data of four cities in the Philippines from 2006-2010 were collected from the PSA-NSO and PAGASA, respectively. In order to observe the risks associated with the heatwaves, we restricted the analysis only for the dry season from December to March of each year. We used a distributed lag non-linear model to characterize the city-specific temperature and all-cause mortality relationship; the data follows a Poisson distribution with over-dispersion.

$$Y_t \sim Poisson\ (\mu_t)$$

$$log[E(Y_t)] = \alpha + \beta_{(t,l)} + s(RH_t, df) + s(time_t) + DOW_t + Holiday_t$$

The mean temperature effect constitutes the pooled city-specific results across the cities and was analyzed through random effect meta-analysis. Mean temperature effects were based on HW and non-HW days (binary outcome), while sustained HW days were based on duration and intensity. The methodology used in this study is based on the methodological definition by Gasparrini and Armstrong (2011). We invite the readers to examine the paper by Gasparrini and Armstrong (2011) for further reading.

Both the first and second study have showed that high temperature effects were immediate so we used the 2- and 4-day duration on different intensities (97^{th}, 98^{th}, and 99^{th}) as HW definitions, which were also based on previous studies (Anderson and Bell 2009b; Barnett et al. 2012; D'Ippoliti et al. 2010; Gasparrini and Armstrong 2011; Son et al. 2012; Zeng et al. 2014). In simple terms, the HW indicator will count as 1 if the day exceeds the temperature threshold in a given duration, otherwise, 0.

HW effects were also estimated using the same meta-analytic techniques in the mean temperature effects. All statistical analyses were done using R Statistical Programming.

4.2. Results

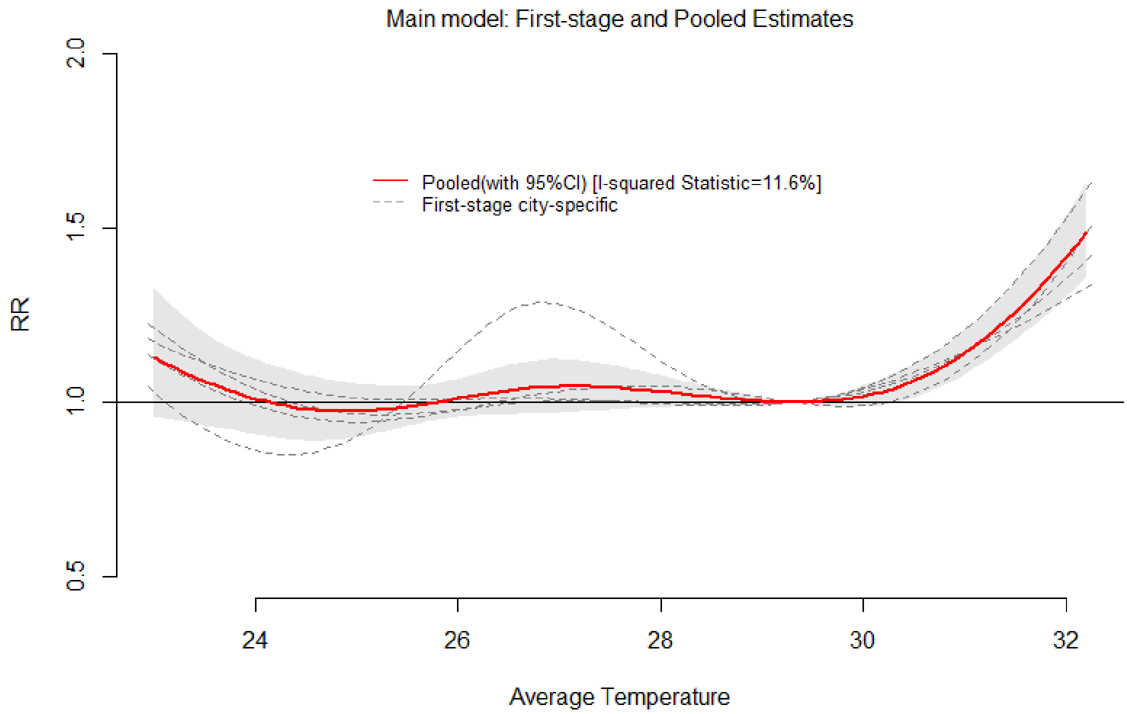

Figure 17. Pooled and city-specific patterns of the mean temperature effects

Figure 17 shows the pooled and city-specific estimates of the mean temperature effects. The read solid line is the pooled pattern, while the dotted gray lines are the city-specific risk curves. Based on I-squared statistics (I-square = 11.6%), there is not much heterogeneity among the cities, hence they are homogeneous.

Table 3. Summary statistics of Heatwave days based on different duration (>2,>4days) and intensity (97^{th}, 98^{th}, 99^{th}) and the total number of days (for the span of 2006-2011)

	Heatwave days						**Total number of days**
	2 days			4 days			
City	97^{th}	98^{th}	99^{th}	97^{th}	98^{th}	99^{th}	
Manila	19	10	6	11	3	2	1826
Cebu	23	18	5	19	14	0	1826
Davao	10	10	4	2	2	0	1826
Quezon	16	10	6	10	4	4	1826

In Table 3, it can be observed that the varying duration and intensity will affect the detection of the HW days. The most HW days recorded can be observed in Cebu for HW days beyond the 97^{th} temperature percentile, and continuing for more than 2 days. It is worthy to note that, as the duration increases, and as the intensity increases, the number of HW days being detected becomes lesser and lesser.

Table 4. Percent increase brought attributed to mean temperature effects and added HW effects in different

duration and intensity among all-cause mortality

Duration	Intensity	% Change Mean temperature effects	95% CI	% Change HW Effects	95% CI
2 days	97th	13.9	2.7 to 26.4	6.5	-1.3 to 14.9
	98th	20.8	3.5 to 41	0.3	-7.8 to 9.2
	99th	24.1	7.2 to 43.5	-4.1	-13.5 to 6.2
4 days	97th	17.5	4.7 to 32	3.8	-5.5 to 14.1
	98th	23.2	8 to 40.5	-0.4	-10.8 to 11.3
	99th	34.9	20.5 to 50.9	-0.5	-14.8 to 16.2

Table 4 shows the percent of increase which can be brought about by either the mean temperature effects or the HW effects. It can be observed that the mean temperature effects contribute a bigger percentage of change to the RR. On the other hand, HW effects contribute negligible change to the RR with negative change mostly observed in the 99th temperature percentile, irrespective of the duration.

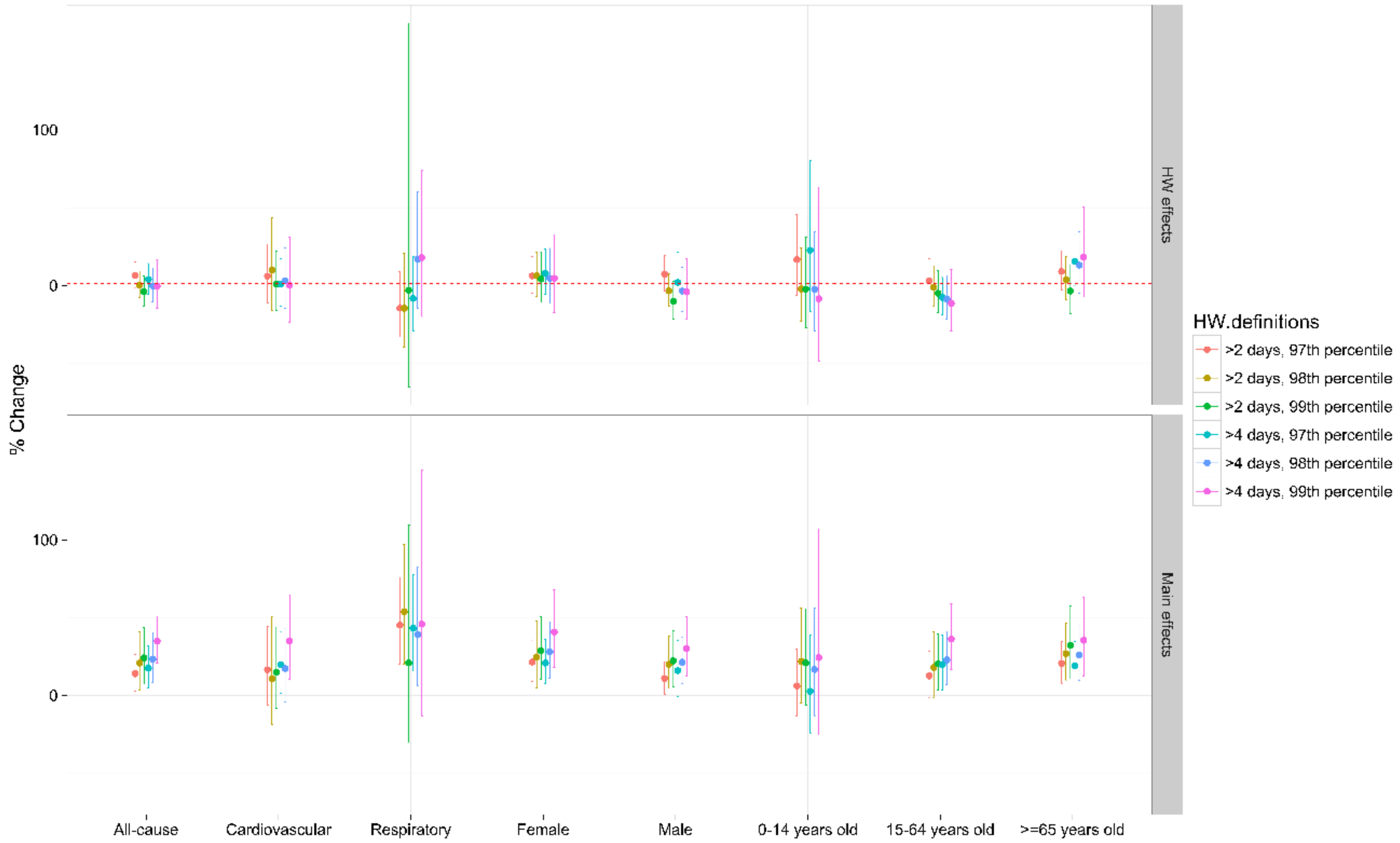

Figure 18. Cause-, sex-, and age-specific percent of change for both mean and HW effects in different mortality subgroups on the varying HW definitions

Figure 18 shows the percent change by the mean temperature effects on the different mortality subgroups, with the greatest risk observed in the respiratory subgroup. It is interesting to note that there is a clear difference between the mean and HW effects with regard to the direction of the risk with respect to the HW definition among the 15-64 years old.

4.3. Discussion

The HW study was able to disentangle the mean temperature effects and the HW effects by identifying the cumulative HW days from non-HW days, and has demonstrated that the mean temperature effects have greater impact on the risk than the HW effects. Likewise, the study was able to determine the differences of the change of risk in the different mortality subgroups.

As seen in Table 17, using the HW indicator defined by Gasparrini and Armstrong (2011), we expect an occasional decrease of the number of the detected HW days as either/both duration and/or intensity increases. Although there might be intense HW events, which may last for a week or more, these events may be rather rare to be considered. It can also be observed in Table 4 as well as in Figure 18, that the mean temperature effects have increasing risks as the duration and percentile increases, while the HW effects decrease with the increased duration and intensity.

Temperature affects the thermoregulatory capacity of the person, in ways which could be detrimental to one’s overall health (Huynen et al. 2001). Extreme heat days, such as HW, may pose even greater risks to the body, which is already at the current state of risk from the usual mean temperature (Barnett et al. 2012). However, the results of this study have shown that the mean temperature effects have greater impact than the HW effect, which is in concurrence to those observed by Gasparrini and Armstrong (2011) and Zeng et al. (2014). This low significance of the HW effects may be attributable to the public health interventions such as health advisories against impending HW days (Zeng et al. 2014). This is also true with the Philippine context, timely announcements are being done during days with unusually high temperatures. As a result, people would prefer to stay indoors and use all possible cooling mechanisms such as fan and air-condition, and sometimes buy cold drinks or food, as a countermeasure for the heat.

Interestingly, we have observed an interesting pattern whereby the effects estimate of the mean temperature effects increases as the intensity increases, on the other hand, the HW effects decreases with intensity, as seen in Table 4. This pattern can also be observed among the risk populations, which is particularly well-pronounced in the 15-64 years old population (in Figure 18). There is no straightforward explanation for this phenomenon, however, we believe that as intensity increases, the HW added effects might have decreased due to the various adaptive capacities, physiological, technological and/or behavioral, which were able to counter the HW effects. Hoffmann et al. (2008) noted that the lack of nightly cooling may contribute to increase mortality during HW days. Similarly, Henschel et al. (1969) observed that when heat accumulates in infrastructures devoid of air conditioning during HW days, this may aggravate certain health complications, such as hyperventilation and dehydration (Son et al. 2012). Building the adaptive capacity premise, if there were to be existing adaptive capacities, then the added HW affect might have been lowered, but such adaptive capacities may not be sufficiently large enough to affect the mean temperature effects, hence the increasing change due to increasing intensity.

In Figure 18, we have observed statistically insignificant changes of the effect modification by the different subgroups. There are different directions of the change brought about by either the mean temperature effects or the HW effects. However, it is worthy to note that the mostly affected populations, having the higher percent change in either mean temperature or HW effects compared to their respective subgroups, belong to the respiratory-related mortality, female, and the elderly (≥65 years old). Previous studies have shown that high temperature may exacerbate chronic pulmonary diseases due to excess heat dissipation through circulatory adjustment (Michelozzi et al. 2009). Some studies have showed that females have higher risks compared to males which may be attributable to socioeconomic factors and geographical context (Hajat et al. 2005; O'Neill 2003). On the other hand, Basu and Ostro (2008) have shown that sex may not play any big difference with the risk. These irreconcilable findings warrant further investigation. We have also observed that the elderly has the greatest risk in the age spectrum due to their decreased thermoregulatory capacity (Seposo et al. 2015, 2016).

CHAPTER 5: STUDY 4 – Estimating the Effects of Mean, Inter-, and Intra-day temperature variations on mortality in the Philippines

Extensive research from countries across the globe have been done with regard to probing the effects of temperature on health, with cascades of studies supporting the non-linear relationship. However, there are ample evidence which have had explored the effects of inter- and intra-day variations (otherwise known as the diurnal temperature range) in relation to mortality, let alone among cause-specific ones. This fourth study, supported by the previous knowledge established by the preceding three studies, focuses in determining the risks associated with the mean, inter- and intra-day temperatures in all-cause and cause-specific mortality.

5.1. Methods

We used a Quasi-Poisson regression coupled with a distributed lag non-linear model (DLNM) in estimating the relative risks (RR) due to (1) mean temperature, (2) inter-day variations, and (Nixdorf-Miller et al.) intra-day variations in all-cause mortality among the cities of the Philippines. We further explored the variations in the risks in both cardiovascular- and respiratory-related mortality. Inter-day variations were calculated based on the difference of the mean temperature between days, while intra-day, otherwise known as diurnal temperature range (DTR), is the difference of the maximum temperature and the minimum temperature of the same day.

Vicedo-Cabrera et al. (2016) have shown that there are variations with regard to the risks are associated with the mean temperature, particularly in the inter- and intra-day variations. Taking this into account, we created 2 indicators for each of the exposure indices (inter- and intra-day variations). Inter-day variations which are greater than the minimum mortality temperature (MMT) are known to be an "increase in temperature" (x_t^{inc}), while those below are known to be a "decrease in temperature" (x_t^{dec}). For intra-day variations greater than MMT, they are known to be as DTR in high temperature days (x_t^{high}), while those lower than the MMT are DTR in low temperature days (x_t^{low}).

First stage city-specific exposure-response curves were modeled using Quasi-Poisson regression, which takes into account over-dispersion, coupled with DLNM using the following equation:

$$\log(\mu_t^c) = \alpha + ns\left(CB_{T,l}^c; \beta\right) + ns(date, 7\times5) + \text{as.factor(dow)} + \gamma x_t^{inc} + \vartheta x_t^{dec} \\ + \rho x_t^{high} + \tau x_t^{low}$$

$\log(\mu_t^c)$ is the log of the expected value of mortality on city *c* on time *t*; α is the intercept; *ns* is the natural cubic spline; $CB_{T,l}^c$ is the cross-basis term per city, on the respective temperature and lag dimensions with 4 df each; β is the vector of the regression coefficients for the crossbasis term; *date* is the year of the observation period with 35 df; *dow* accounts for the day of the week as a categorical variable; γ is the coefficient of the increase in temperature variable (x_t^{inc}) of the inter-day variations; ϑ is the coefficient of the decrease in temperature variable (x_t^{inc}) of the inter-day variations; ρ is the coefficient of the DTR in high temperature days variable (x_t^{high}); τ is the coefficient of the DTR in low temperature days variable (x_t^{low}).

5.2. Results

Table 5. Meteorological and mortality variables of the four cities in the Philippines, 2006-2010

Variables	Manila Philippines			Cebu Philippines			Davao Philippines			Quezon City Philippines		
	Mean (±SD)	Min	Max	Mean (±SD)	Min	Max	Mean (±SD)	Min	Max	Mean (±SD)	Min	Max
All-cause mortality	52 ± 8.4	14	81	24 ± 5.5	9	45	24 ± 5.3	10	46	51 ± 8.3	27	92
Cardiovascular-related mortality	15 ± 4.0	1	29	7.3 ± 2.9	0	19	8.7 ± 3.3	0	22	17 ± 4.3	4	32
Respiratory-related mortality	6.4 ± 2.8	0	18	2.6 ± 1.7	0	9	2.1 ± 1.6	0	10	6.0 ± 2.6	0	18
Minimum temperature (°C)	26 ± 1.5	18	31	25 ± 1.2	14	28	24 ± 0.8	16	27	23 ± 1.6	12	28
Mean temperature (°C)	29 ± 1.5	23	33	28 ± 1.2	22	32	28 ± 1.1	23	31	27 ± 1.6	22	32
Maximum temperature (°C)	32 ± 1.9	23	37	31 ± 1.6	24	41	32 ± 1.6	24	39	32 ± 2.2	24	38
Inter-day temperature change (°C)												
Increase in temperature	0.1 ± 0.3	0	2.5	0.1 ± 0.3	0	2.2	0.4 ± 0.6	0	4.1	0.2 ± 0.4	0	3.1
Decrease in temperature	0.3 ± 0.5	0	4.2	0.2 ± 0.5	0	5.7	0 ± 0.1	0	1.6	0.2 ± 0.5	0	4.3
Intra-day temperature change (°C)												
DTR on hot days	2.5 ± 3.3	0	17	3.5 ± 3.6	0	17	7.8 ± 1.7	0	18	4.5 ± 4.8	0	16
DTR on cold days	3.3 ± 3.0	0	13	2.9 ± 3.2	0	15	0 ± 0.3	0	5.3	4.2 ± 4.4	0	18
Relative Humidity	74 ± 7.5	53	100	83 ± 5.4	57	100	82 ± 4.3	67	100	78 ± 8.2	40	99

Table 5 shows the summary table of both meteorological and mortality variables together with the inter- and intra-day variables. Most of the all-cause mortality can be observed in Manila and Quezon cities; 52 ± 8.4 and 51 ± 8.3, respectively. While the mean temperature among the cities are comparably similar to each other (Manila = 29 ± 1.5; Cebu = 28 ± 1.2; Davao = 28 ± 1.1; Quezon = 27 ± 1.6).

Table 6. Relative risk estimates of the association of mortality and mean daily temperature and Inter-day and Intraday variations

	Manila Philippines			Cebu Philippines			Davao Philippines			Quezon City Philippines		
	RR	95%	CI	RR	95%	CI	RR	95%	CI	RR	95%	CI
Mean daily temperature												
Heat	1.35	1.21	1.51	1.20	1.03	1.39	1.11	0.92	1.34	1.34	1.21	1.49
Cold	1.11	0.93	1.32	0.90	0.70	1.16	0.76	0.52	1.11	1.15	1.01	1.30
Inter-day Δ in temperature												
Increase in temperature	0.98	0.96	1.00	1.03	0.99	1.06	1.02	0.99	1.06	0.99	0.97	1.02
Decrease in temperature	1.00	0.99	1.02	1.01	0.99	1.03	1.00	0.97	1.02	0.99	0.98	1.01
Intra-day Δ in temperature												
DTR on low temp days	1.01	0.96	1.05	1.02	0.96	1.09	1.02	0.96	1.08	1.06	1.01	1.11
DTR on high temp days	1.02	0.99	1.05	1.01	0.97	1.06	1.03	0.98	1.08	1.03	0.99	1.06

Δ ≡ change

Table 6 shows the RR of the mean daily temperature, inter- and intra-day variations together with the various indices. High risks were observed in the mean daily temperature, while either low risks or protective effects can be seen on both the inter- and intra-day variations.

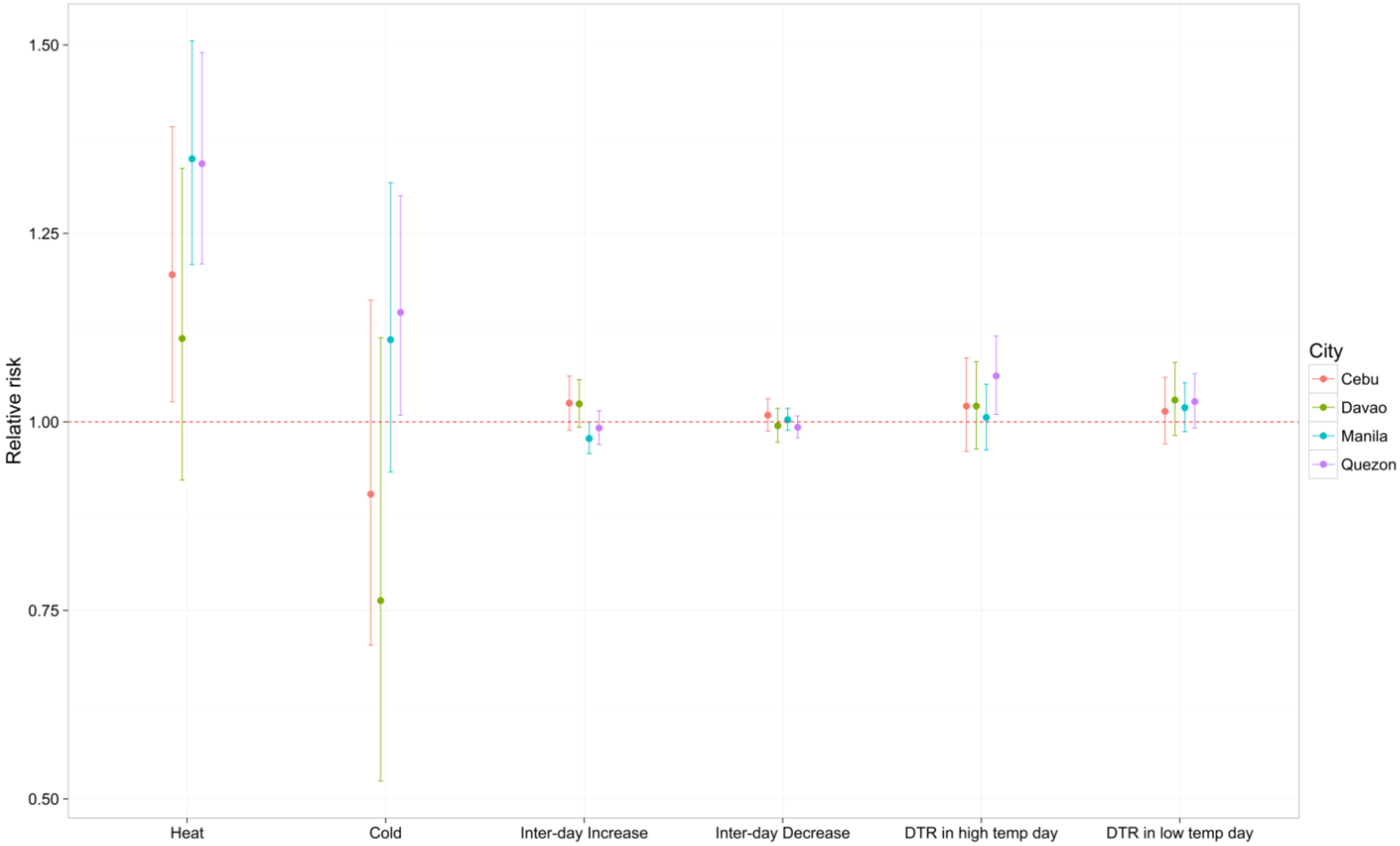

Figure 19. RR of the all-cause mortality of the various temperature indices

Figure 19 shows the RR of all-cause mortality of the various temperature indices in the different cities. Both the heat and cold effects are higher than remaining temperatures indices. Both Manila and Quezon recorded higher risks in both heat and cold effects, compared to the other cities.

Figure 20. Log of the RR in either cardiovascular- and respiratory-related mortality

Figure 20 shows the log of the RR of the cause-specific mortality of the different cities in the various indices. Higher risks are observed among the cardiovascular-related mortality during low temperature days, while risks are inclined during the high temperature days among respiratory-related mortality subgroup. We opted to use the log of the RR due to the relatively wide confidence intervals of the estimates.

5.3. Discussion

Numerous studies have explored the effects of DTR on mortality or morbidity (Cao et al. 2009; Chen et al. 2007; Chu et al. 2011; Ding et al. 2015; Ding et al. 2016; Holopainen et al. 2014; Kan et al. 2007). Some of the studies have observed a linear relationship (Lim et al. 2012b; Lim et al. 2015; Wang et al. 2013; Zhou et al. 2014), while others have recorded non-linear associations of DTR with either mortality/morbidity (Ding et al. 2015; Luo et al. 2013). However, only a few studies have tried to differentiate the effects by the mean temperature, inter- and intra-day variations from each other (Vicedo-Cabrera et al. 2016). Likewise, only a few studies have explored the effect modification brought about by the mortality subgroups (Ding et al. 2016; Luo et al. 2013; Wang et al. 2013; Zheng et al. 2016). This study aimed to determine the risks associated with the different exposure indices, and was able to establish the following findings: 1) mean temperature effects have higher effects estimate compared to that of the inter- or intra-day variations, and that 2) the pronounced effects of mean temperature is also true with the cardiovascular- and respiratory-related mortality, with respiratory-related populations experiencing greater risks during high temperature days.

The result of mean temperature effects having greater risk compared to the inter- and inter-day variations is similar to that observed by Vicedo-Cabrera et al. (2016). Since the temperature range in the Philippines is not that wide, the intra-day or inter-day variations may not be that large enough to significantly affect the risks. Likewise, technological or behavioral adaptation (McMichael et al. 2008) may have played a role with regard the lesser risk or protective effect observed among the cities, in cases whereby the population are informed due to real-time forecasting about the current weather scenario, or when air conditioning is used (Medina-Ramon and Schwartz 2007a; Nordio et al. 2015). However, there might be other factors which were not accounted in this study, in contrast to those studies which found significant effects (Kan et al. 2007; Lim et al. 2015), which warrant further investigation.

Same with the all-cause mortality, cause-specific mortality has greater risk in the mean temperature compared with that of the inter- and intra-day variations. This is in contrast with the findings by Kan et al. (2007), whereby there is an 1.86% (95% CI: 1.40-2.32%) increase in the cardiovascular mortality and a 1.29% (95% CI: 0.49-2.09%) increase in respiratory mortality for the intra-day variable, DTR. Similar findings were observed by Lim et al. (2012a) wherein the risk of hospital admissions for various cardiovascular diseases showed that DTR had adverse effect on cardiac failure with an effect estimates of 3.0% (95% CI: 1.4-4.6). The statistically insignificant effects estimate of both inter- and intra-day variations may be justified by the adaptive capacities. Kim et al. (2016) noted that populations might have adapted to the DTR variations, hence, the statistically non-significance of the effects estimate. Similar assumptions can be used for inter-day variations, which led to the same level of statistical insignificance. Clearly, adaptive capacities may have played a role in the aforementioned contexts, however, due to the lack of the proper definition and conceptual framework of adaptation, we were unable to verify these assumptions.

CHAPTER 6: Overview

6.1. Highlights of Studies

In study 1, temperature-mortality relationship in Manila City was observed to have elevated risks of mortality in the elderly, female, and respiratory-causes. This study serves as a cornerstone for category-specific policies in addressing the effects of temperature on health. Patterns observed in the seasonal analysis can be used as baseline for future studies regarding leptospirosis and diarrhea which might have introduced confounding.

While in study 2, effect modification by mortality subgroups were evident in the extreme temperatures of tropical cities, and that health-related policies should take these variations in the risks into consideration in order to create strategies with respect to the population-at-risk. In particular, strategies which include an increase cooling through the access of air-condition units (O'Neill and Ebi 2009) for the elderly, or the timely awareness and education campaigns (Sheridan 2007) for the specific risk populations can help avert risks at a certain extent.

In a general perspective, there are numerous strategies which apply to not just the risk population, but also to the general public, such as: improving an infrastructure’s thermal insulation (Analitis et al. 2008) and installation of early warning systems for heat surveillance (Ebi and Schmier 2005), which can also be done in parallel with the strategies in targeting the risk populations.

In study 3, we were able to disentangle the mean temperature effects from the HW effects using different HW definitions. The mean temperature effects largely affect the change in the risk compared to that of the HW effects. Regardless of the effects group (mean temperature or HW), strategies should be directed toward the vulnerable populations; respiratory-related, female and elderly.

Lastly, in study 4, we were able to establish the need for well-concerted focus towards the effects of the mean temperature towards health aside from the other heat indices. Although we were not able to find significant risks associated with either all-cause and cause-specific mortality and that of the inter- and intra-day variations, other factors not accounted in the study such as adaptation should be taken into consideration for future work.

6.2. Strength of the Studies and future direction

Each study can be a standalone, but can also be patterned in an overall framework of assessing the associations of temperature and mortality in the Philippines. Each study has its own strength which contributes to the overall strength of this manuscript. The initial study was the first study to be conducted in the Philippines, and has given a better insight of the risks with temperature in relation to mortality. The second study has further strengthened the initial findings, whereby risk groups should be considered whenever dealing with the risks, and not just from a general population's risk. The second study was also able to establish the risks with respect to the temperature gradient; extreme low temperature, moderate low temperature, moderate high temperature, and extreme high temperature, which further enabled a better understanding of the effect modification by mortality subgroups in different temperature percentiles. The third and fourth studies have been able to establish the major contribution of mean temperature in comparison to other temperature indices, such as HW, inter- and intra-day variations, to the risk or susceptibility of a person.

The collection of studies has highlighted the risk curves in a tropical setting, identified the risk populations being affected, and emphasized the higher risks posed by the mean temperature. In the process of conducting these research studies, we have identified some plausible underlying mechanisms which could pave way for new research directions in this field. In the first study, we believe that there might be possible confounding by diarrhea, which brings forth a new perspective of including infectious disease dynamics into the temperature-mortality relationships. Both the statistically insignificant observations in the third and fourth study can be possibly linked towards the notion of adaptation. Adaptation dynamics involves the adjustment of the either natural or human systems in response to a given stimulus in order to moderate harm (IPCC 2007). Current research have been geared towards the identification of possible representations, which can be used to proxy for adaptation, and observe how various types of adaptation affects the temperature-mortality relationship (Arbuthnott et al. 2016; Barreca et al. 2016; Bobb et al. 2014). We believe that by incorporating and exploring the mechanisms of infectious diseases and adaptation with respect to the temperature-mortality relationship, can forge new research directions, which are essential in understanding the previously observed risks/relationships/patterns.

6.3. Limitations of the Studies

Though we have already highlighted the strengths of these studies, there are unavoidable limitations, which we would like to acknowledge in this manuscript. First, the risk curves observed in the selected cities in this study can't be generalized into the other cities in the country. Each city has its own city-specific characteristic, which may influence risk. Second, were not able to incorporate air pollution data into the modeling due to data unavailability. Third, we were not able to fully separate all-cause mortality to even finer groupings of mortality by cause of death due to the sparseness of the current data. Lastly, there is a limitation to the number of cities included due to the existence of only a handful of government-operated weather stations monitoring the respective meteorological variables.

6.4. Policy Implications

Each of the studies has highlighted the need to address the risks attributed to the temperature-mortality association in different, yet unifying perspective, with each (study) being a standalone study, but can be unified into the whole framework of risk profiling. The key messages from each study have been consolidated to the following points:

1. Risks in tropical cities have been observed also in the low temperature extremes, hence, these should also be taken into consideration for planning relevant warning systems;
2. Risks in these tropical cities were observed to be prominently affected by mean temperature in either low or high temperature extremes, which calls upon greater focus on the effects brought upon by such temperature index;

3. In planning strategies, the risks per risk population should also be factored in, since they experience different intensities of the risks compared to the whole population; and,
4. The understanding for heatwaves as well as the other pertinent temperature indices such as inter- and intra-day variations and their roles in the temperature-mortality relationship, are not sufficient enough to explain their lack of significance or even the observed protective effects compared to other studies, hence, more detailed studies should be carried out taking into account other plausible variables which can affect such results, such as adaptation.

These findings provide a comprehensive profiling of the risks associated with the temperature-mortality relationship. We believe that the results of these studies, and the overall profiling can serve as a guide to policymakers, as well as to other relevant stakeholders, to enjoin them to not only improve the early warning signs in recognizing the effects of climate change on health, but also to prepare the risk populations towards such impending risks.

CHAPTER 7: Conclusions

This dissertation thesis was able to comprehensively address the fundamental issues in relation to quantifying the effects and the extent of effects of climate change, particularly of temperature, on health. Specifically, we were able to determine the relationship of temperature on mortality among the tropical cities. Likewise, effect modification was evident when all-cause mortality is divided further into subgroups, in which, females, patients with respiratory illnesses, and elderly people have greater risks compared to their respective counterparts. Further analyses showed that mean temperature has greater impact compared to emerging temperature indices such as HW, inter- and intra-day variations. This only shows that greater focus should be allotted to mean temperature and its effect on human health, and also take into account the risk variations with respect to the specific population-at-risk. The results of the respective studies, taken in parts or as a whole, can now be laid as a foundation to current and future environmental health strategic frameworks in addressing the effects of climate change. This profiling of risk is essential in crafting policy-oriented roadmaps and also to tailor-fit strategies relevant to the specific population-at-risk.

Publication Notes

The first two studies, risk determination study and effect modification by mortality subgroups study have been published in 2015 and 2016, respectively. On the other hand, the heatwave and the mean, inter- and intra-day variations studies are currently included as part of the collaborative research, and are both under review with the respective journals, both with the expected publication in either late 2016 or early 2017.

References

Analitis A, Katsouyanni K, Biggeri A, Baccini M, Forsberg B, Bisanti L, et al. 2008. Effects of Cold Weather on Mortality: Results From 15 European Cities Within the PHEWE Project. American journal of epidemiology 168:1397-1408.

Anderson BG, Bell ML. 2009a. Weather-related mortality: how heat, cold, and heat waves affect mortality in the United States. Epidemiology 20:205-213.

Anderson BG, Bell ML. 2009b. Weather-Related Mortality How Heat, Cold, and Heat Waves Affect Mortality in the United States. Epidemiology 20:205-213.

Arbuthnott K, Hajat S, Heaviside C, Vardoulakis S. 2016. Changes in population susceptibility to heat and cold over time: assessing adaptation to climate change. Environmental health : a global access science source 15 Suppl 1:33.

Armstrong B, Gasparrini A. 2012. Time series regression: advancements in this new tool for epidemiological analyses.

Ballester F, Corella D, PerezHoyos S, Saez M, Hervas A. 1997. Mortality as a function of temperature. A study in Valencia, Spain, 1991-1993. International Journal of Epidemiology 26:551-561.

Barnett AG, Hajat S, Gasparrini A, Rocklov J. 2012. Cold and heat waves in the United States. Environmental research 112:218-224.

Barreca A, Clay K, Deschenes O, Greenstone M, Shapiro JS. 2016. Adapting to Climate Change: The Remarkable Decline in the US Temperature-Mortality Relationship over the Twentieth Century. Journal of Political Economy 124:105-159.

Basu R, Dominici F, Samet JM. 2005. Temperature and mortality among the elderly in the United States: a comparison of epidemiologic methods. Epidemiology 16:58-66.

Basu R, Ostro BD. 2008. A multicounty analysis identifying the populations vulnerable to mortality associated with high ambient temperature in California. American journal of epidemiology 168:632-637.

Basu R. 2009. High ambient temperature and mortality: a review of epidemiologic studies from 2001 to 2008. Environmental health : a global access science source 8:40.

Bell ML, O'Neill MS, Ranjit N, Borja-Aburto VH, Cifuentes LA, Gouveia NC. 2008. Vulnerability to heat-related mortality in Latin America: a case-crossover study in Sao Paulo, Brazil, Santiago, Chile and Mexico City, Mexico. International journal of epidemiology 37:796-804.

Bobb JF, Peng RD, Bell ML, Dominici F. 2014. Heat-related mortality and adaptation to heat in the United States. Environmental health perspectives 122:811-816.

Breitner S, Wolf K, Devlin RB, Diaz-Sanchez D, Peters A, Schneider A. 2014. Short-term effects of air temperature on mortality and effect modification by air pollution in three cities of Bavaria, Germany: A time-series analysis. Science of the Total Environment 485:49-61.

Cao J, Cheng Y, Zhao N, Song W, Jiang C, Chen R, et al. 2009. Diurnal temperature range is a risk factor for coronary heart disease death. J Epidemiol 19:328-332.

Carlton EJ, Eisenberg JN, Goldstick J, Cevallos W, Trostle J, Levy K. 2014. Heavy rainfall events and diarrhea incidence: the role of social and environmental factors. American journal of epidemiology 179:344-352.

Chadsuthi S, Modchang C, Lenbury Y, Iamsirithaworn S, Triampo W. 2012. Modeling seasonal leptospirosis transmission and its association with rainfall and temperature in Thailand using time-series and ARIMAX analyses. Asian Pac J Trop Med 5:539-546.

Chen G, Zhang Y, Song G, Jiang L, Zhao N, Chen B, et al. 2007. Is diurnal temperature range a risk factor for acute stroke death? Int J Cardiol 116:408-409.

Chu C, Zhou W, Gui Y, Kan H. 2011. Diurnal temperature range as a novel risk factor for sudden infant death. Biomedical and environmental sciences : BES 24:518-522.

Chung JY, Honda Y, Hong YC, Pan XC, Guo YL, Kim H. 2009. Ambient temperature and mortality: an international study in four capital cities of East Asia. The Science of the total environment 408:390-396.

Cinco TA, Hilario FD, De Guzman RG, Ares ED. 2013. CLIMATE TRENDS AND PROJECTIONS IN THE PHILIPPINES. In: 12th National Convention on Statistics (NCS). Quezon City, Philippines:Philippine Atmospheric, Geophysical and Astronomical Services Administration (PAGASA), 20.

Cinco TA, de Guzman RG, Hilario FD, Wilson DM. 2014. Long-term trends and extremes in observed daily precipitation and near surface air temperature in the Philippines for the period 1951–2010. Atmospheric Research 145-146:12-26.

Curriero FC, Heiner KS, Samet JM, Zeger SL, Strug L, Patz JA. 2002. Temperature and mortality in 11 cities of the eastern United States. Am J Epidemiol 155:80-87.

D'Ippoliti D, Michelozzi P, Marino C, de'Donato F, Menne B, Katsouyanni K, et al. 2010. The impact of heat waves on mortality in 9 European cities: results from the EuroHEAT project. Environ Health-Glob 9.

Ding Z, Guo P, Xie F, Chu HF, Li K, Pu JB, et al. 2015. Impact of diurnal temperature range on mortality in a high plateau area in southwest China: A time series analysis. Science of the Total Environment 526:358-365.

Ding Z, Li LJ, Xin LY, Pi FH, Dong WY, Wen Y, et al. 2016. High diurnal temperature range and mortality: Effect modification by individual characteristics and mortality causes in a case-only analysis. Science of the Total Environment 544:627-634.

DOH. 2010. Philippine National Environmental Health Action Plan. Manila, Philippines:Department of Health.

Downing RG, Otten RA, Marum E, Biryahwaho B, Alwano-Edyegu MG, Sempala SDK, et al. 1998. Optimizing the delivery of hiv counseling and testing services: The uganda experience using rapid hiv antibody test algorithms. J Acq Immun Def Synd 18:384-388.

Ebi KL, Teisberg TJ, Kalkstein LS, Robinson L, Weiher RF. 2004. Heat Watch/Warning Systems Save Lives: Estimated Costs and Benefits for Philadelphia 1995–98. B Am Meteorol Soc 85:1067-1073.

Ebi KL, Schmier JK. 2005. A Stitch in Time: Improving Public Health Early Warning Systems for Extreme Weather Events. Epidemiol Rev 27:115-121.

El-Zein A, Tewtel-Salem M, Nehme G. 2004. A time-series analysis of mortality and air temperature in Greater Beirut. Science of the Total Environment 330:71-80.

Gasparrini A, Armstrong B, Kenward MG. 2010. Distributed lag non-linear models. Statistics in medicine 29:2224-2234.

Gasparrini A. 2011. Distributed Lag Linear and Non-Linear Models in R: The Package dlnm. J Stat Softw 43:1-20.

Gasparrini A, Armstrong B. 2011. The impact of heat waves on mortality. Epidemiology 22:68-73.

Gasparrini A, Armstrong B, Kovats S, Wilkinson P. 2012. The effect of high temperatures on cause-specific mortality in England and Wales. Occupational and environmental medicine 69:56-61.

Gasparrini A, Armstrong B. 2013. Reducing and meta-analysing estimates from distributed lag non-linear models. Bmc Med Res Methodol 13.

Gasparrini A. 2014. Modeling exposure-lag-response associations with distributed lag non-linear models. Statistics in medicine 33:881-899.

Gasparrini A, Guo YM, Hashizume M, Lavigne E, Zanobetti A, Schwartz J, et al. 2015. Mortality risk attributable to high and low ambient temperature: a multicountry observational study. Lancet 386:369-375.

Goodman PG, Dockery DW, Clancy L. 2004. Cause-specific mortality and the extended effects of particulate pollution and temperature exposure. Environmental health perspectives 112:179-185.

Gouveia N. 2003. Socioeconomic differentials in the temperature-mortality relationship in Sao Paulo, Brazil. International Journal of Epidemiology 32:390-397.

Gouveia N, Hajat S, Armstrong B. 2003. Socioeconomic differentials in the temperature-mortality relationship in Sao Paulo, Brazil. International Journal of Epidemiology 32:390-397.

Guo Y, Barnett AG, Pan X, Yu W, Tong S. 2011. The impact of temperature on mortality in Tianjin, China: a case-crossover design with a distributed lag nonlinear model. Environmental health perspectives 119:1719-1725.

Guo Y, Barnett AG, Tong S. 2013. Spatiotemporal model or time series model for assessing city-wide temperature effects on mortality? Environmental research 120:55-62.

Guo Y, Gasparrini A, Armstrong B, Li SS, Tawatsupa B, Tobias A, et al. 2014a. Global Variation in the Effects of Ambient Temperature on Mortality A Systematic Evaluation. Epidemiology 25:781-789.

Guo Y, Li S, Tawatsupa B, Punnasiri K, Jaakkola JJ, Williams G. 2014b. The association between air pollution and mortality in Thailand. Scientific reports 4:5509.

Ha J, Kim H, Hajat S. 2011a. Effect of Previous-Winter Mortality on the Association between Summer Temperature and Mortality in South Korea. Environmental health perspectives 119:542-546.

Ha J, Shin Y, Kim H. 2011b. Distributed lag effects in the relationship between temperature and mortality in three major cities in South Korea. Science of the Total Environment 409:3274-3280.

Hajat S, Armstrong BG, Gouveia N, Wilkinson P. 2005. Mortality displacement of heat-related deaths - A comparison of Delhi, Sao Paulo, and London. Epidemiology 16:613-620.

Hales S, Edwards SJ, Kovats RS. 2014. Impacts on health of climate extremes. In: Quantitative risk assessment of the effects of climate change on selected causes of death, 2030s and 2050s, (Hales S, Kovats, S., Lloyd, S., and Campbell-Lendrum, D., ed). Switzerland:WHO Press.

Harlan SL, Declet-Barreto JH, Stefanov WL, Petitti DB. 2013. Neighborhood effects on heat deaths: social and environmental predictors of vulnerability in Maricopa County, Arizona. Environmental health perspectives 121:197-204.

Havenith G. 2005. Temperature regulation, heat balance and climatic stress. Extreme Weather Events and Public Health Responses:69-80.

Henschel A, Burton LL, Margolies L, Smith JE. 1969. An analysis of the heat deaths in St. Louis during July, 1966. Am J Public Health Nations Health 59:2232-2242.

Hoffmann B, Hertel S, Boes T, Weiland D, Jockel KH. 2008. Increased cause-specific mortality associated with 2003 heat wave in Essen, Germany. J Toxicol Environ Health A 71:759-765.

Holopainen J, Helama S, Partonen T. 2014. Does diurnal temperature range influence seasonal suicide mortality? Assessment of daily data of the Helsinki metropolitan area from 1973 to 2010. International journal of biometeorology 58:1039-1045.

Huang W, Kan H, Kovats S. 2010. The impact of the 2003 heat wave on mortality in Shanghai, China. The Science of the total environment 408:2418-2420.

Huynen MMTE, Martens P, Schram D, Weijenberg MP, Kunst AE. 2001. The impact of heat waves and cold spells on mortality rates in the Dutch population. Environmental health perspectives 109:463-470.

ICSU and ISSC. 2015. Review of Targets for the Sustainable Development Goals: The Science Perspective.International Council for Science.

IPCC. 2007. Climate Change 2007: Impacts, Adaptation, and Vulnerability. Contribution of Working Group II to the Fourth Assessment Report of the Intergovernmental Panel on Climate Change. Cambridge, UK:IPCC.

Ishigami A, Hajat S, Kovats RS, Bisanti L, Rognoni M, Russo A, et al. 2008. An ecological time-series study of heat-related mortality in three European cities. Environmental health : a global access science source 7:5.

Jhun I, Fann N, Zanobetti A, Hubbell B. 2014. Effect modification of ozone-related mortality risks by temperature in 97 US cities. Environment international 73:128-134.

Kaiser R, Schwartz J, Gotway CA, Rubin CH. 2002. The effect of the Chicago 1995 Heat Wave on all cause and cause-specific mortality. Epidemiology 13:S219-S219.

Kan H, London SJ, Chen HL, Song GX, Chen GH, Jiang LL, et al. 2007. Diurnal temperature range and daily mortality in Shanghai, China. Environmental research 103:424-431.

Kazman JB, Purvis DL, Heled Y, Lisman P, Atias D, Van Arsdale S, et al. 2015. Women and exertional heat illness: identification of gender specific risk factors. US Army Med Dep J:58-66.

Kim J, Shin J, Lim YH, Honda Y, Hashizume M, Guo YL, et al. 2016. Comprehensive approach to understand the association between diurnal temperature range and mortality in East Asia. The Science of the total environment 539:313-321.

Kim Y, Kim H, Kim DS. 2011. Association between daily environmental temperature and suicide mortality in Korea (2001-2005). Psychiatry Res 186:390-396.

Likhvar V, Honda Y, Ono M. 2011. Relation between temperature and suicide mortality in Japan in the presence of other confounding factors using time-series analysis with a semiparametric approach. Environ Health Prev Med 16:36-43.

Lim YH, Hong YC, Kim H. 2012a. Effects of diurnal temperature range on cardiovascular and respiratory hospital admissions in Korea. Science of the Total Environment 417:55-60.

Lim YH, Park AK, Kim H. 2012b. Modifiers of diurnal temperature range and mortality association in six Korean cities. International journal of biometeorology 56:33-42.

Lim YH, Reid CE, Mann JK, Jerrett M, Kim H. 2015. Diurnal temperature range and short-term mortality in large US communities. International journal of biometeorology 59:1311-1319.

Lin YK, Ho TJ, Wang YC. 2011. Mortality risk associated with temperature and prolonged temperature extremes in elderly populations in Taiwan. Environmental research 111:1156-1163.

Liu LQ, Breitner S, Pan XC, Franck U, Leitte AM, Wiedensohler A, et al. 2011. Associations between air temperature and cardio-respiratory mortality in the urban area of Beijing, China: a time-series analysis. Environ Health-Glob 10.

Luo Y, Zhang YH, Liu T, Rutherford S, Xu YJ, Xu XJ, et al. 2013. Lagged Effect of Diurnal Temperature Range on Mortality in a Subtropical Megacity of China. PloS one 8.

Ma W, Zeng W, Zhou M, Wang L, Rutherford S, Lin H, et al. 2015. The short-term effect of heat waves on mortality and its modifiers in China: An analysis from 66 communities. Environment international 75:103-109.

McMichael AJ, Wilkinson P, Kovats RS, Pattenden S, Hajat S, Armstrong B, et al. 2008. International study of temperature, heat and urban mortality: the 'ISOTHURM' project. International journal of epidemiology 37:1121-1131.

Medina-Ramon M, Zanobetti A, Cavanagh DP, Schwartz J. 2006a. Extreme temperatures and mortality: assessing effect modification by personal characteristics and specific cause of death in a multi-city case-only analysis. Environmental health perspectives 114:1331-1336.

Medina-Ramon M, Zanobetti A, Cavanagh DP, Schwartz J. 2006b. Extreme temperatures and mortality: Assessing effect modification by personal characteristics and specific cause of death in a multi-city case-only analysis. Environmental health perspectives 114:1331-1336.

Medina-Ramon M, Schwartz J. 2007a. Temperature, temperature extremes, and mortality: a study of acclimatisation and effect modification in 50 US cities. Occupational and environmental medicine 64:827-833.

Medina-Ramon M, Schwartz J. 2007b. Temperature, temperature extremes, and mortality: a study of acclimatisation and effect modification in 50 US cities. Occupational and environmental medicine 64:827-833.

Michelozzi P, Accetta G, De Sario M, D'Ippoliti D, Marino C, Baccini M, et al. 2009. High temperature and hospitalizations for cardiovascular and respiratory causes in 12 European cities. American journal of respiratory and critical care medicine 179:383-389.

Motohashi Y, Takano T, Nakamura K, Nakata K, Tanaka M. 1996. Seasonality of mortality in Sri Lanka: biometeorological considerations. International journal of biometeorology 39:121-126.

NEC. 2009. Philippine Integrated Disease Surveillance and Response (PIDSR) Annual Report 2009. Manila:Department of Health.

Nitschke M, Tucker G, Hansen A, Williams S, Zhang Y, Bi P. 2016. Evaluation of a heat warning system in Adelaide, South Australia, using case-series analysis. BMJ open 6:e012125.

Nixdorf-Miller A, Hunsaker DM, Hunsaker JC, 3rd. 2006. Hypothermia and hyperthermia medicolegal investigation of morbidity and mortality from exposure to environmental temperature extremes. Arch Pathol Lab Med 130:1297-1304.

Nordio F, Zanobetti A, Colicino E, Kloog I, Schwartz J. 2015. Changing patterns of the temperature-mortality association by time and location in the US, and implications for climate change. Environment international 81:80-86.

O'Neill MS. 2003. Modifiers of the Temperature and Mortality Association in Seven US Cities. American journal of epidemiology 157:1074-1082.

O'Neill MS, Zanobetti A, Schwartz J. 2003. Modifiers of the temperature and mortality association in seven US cities. American journal of epidemiology 157:1074-1082.

O'Neill MS, Ebi KL. 2009. Temperature extremes and health: impacts of climate variability and change in the United States. J Occup Environ Med 51:13-25.

Plavcova E, Kysely J. 2010. Relationships between sudden weather changes in summer and mortality in the Czech Republic, 1986-2005. International journal of biometeorology 54:539-551.

Portier CJ, Thigpen Tart K, Carter SR, Dilworth CH, Grambsch AE, Gohlke J, et al. 2010. A Human Health Perspective On Climate Change: A Report Outlining the Research Needs on the Human Health Effects of Climate Change. Research Triangle Park, NC:Environmental Health Perspectives/National Institute of Environmental Health Sciences.

PSA-PhilSIS. 2014. Exogenous Factors: Monthly Rainfall. Available: http://philfsis.psa.gov.ph/index.php/id/15/matrix/COMFSMRIU7I1URRP201502211242 [accessed March 3, 2015 2015].

RA9729. 2009. Climate Change Act of 2009. Philippines.

Seposo XT, Dang TN, Honda Y. 2015. Evaluating the Effects of Temperature on Mortality in Manila City (Philippines) from 2006-2010 Using a Distributed Lag Nonlinear Model. Int J Environ Res Public Health 12:6842-6857.

Seposo XT, Dang TN, Honda Y. 2016. Effect modification in the temperature extremes by mortality subgroups among the tropical cities of the Philippines. Global health action 9:31500.

Sheridan SC. 2007. A survey of public perception and response to heat warnings across four North American cities: an evaluation of municipal effectiveness. International journal of biometeorology 52:3-15.

Son JY, Lee JT, Anderson GB, Bell ML. 2012. The impact of heat waves on mortality in seven major cities in Korea. Environmental health perspectives 120:566-571.

Stafoggia M, Forastiere F, Michelozzi P, Perucci CA. 2009. Summer Temperature-related Mortality Effect Modification by Previous Winter Mortality. Epidemiology 20:575-583.

Tolentino PL, Poortinga A, Kanamaru H, Keesstra S, Maroulis J, David CP, et al. 2016. Projected Impact of Climate Change on Hydrological Regimes in the Philippines. PloS one 11:e0163941.

Vicedo-Cabrera AM, Forsberg B, Tobias A, Zanobetti A, Schwartz J, Armstrong B, et al. 2016. Associations of Inter- and Intraday Temperature Change With Mortality. American journal of epidemiology 183:286-293.

Villafuerte MQ, Matsumoto J, Akasaka I, Takahashi HG, Kubota H, Cinco TA. 2014. Long-term trends and variability of rainfall extremes in the Philippines. Atmospheric Research 137:1-13.

Wang MZ, Zheng S, He SL, Li B, Teng HJ, Wang SG, et al. 2013. The association between diurnal temperature range and emergency room admissions for cardiovascular, respiratory, digestive and genitourinary disease among the elderly: A time series study. Science of the Total Environment 456:370-375.

WHO-WPRO. 2011. Philippines. 14.

WHO, DOH-Philippines. 2012. Health Service Delivery Profile - Philippines.WHO.

Wilkinson P, Campbell-Lendrum, D.H. and C.L., Bartlett. 2014. Monitoring the health effects of climate change. In: Quantitative risk assessment of the effects of climate change on selected causes of death, 2030s and 2050s, (Hates S, Kovats, S., Lloyd, S., and D. Campbell-Lendrum, ed). 2014:WHO Press.

WMO-WHO. 2015. Heatwaves and Health: Guidance on Warning-System Development.World Meteorological Organization - World Health Organization.

Xiang J, Bi P, Pisaniello D, Hansen A. 2014. The impact of heatwaves on workers' health and safety in Adelaide, South Australia. Environmental research 133:90-95.

Yang J, Ou CQ, Ding Y, Zhou YX, Chen PY. 2012. Daily temperature and mortality: a study of distributed lag non-linear effect and effect modification in Guangzhou. Environ Health-Glob 11.

Zeng W, Lao X, Rutherford S, Xu Y, Xu X, Lin H, et al. 2014. The effect of heat waves on mortality and effect modifiers in four communities of Guangdong Province, China. The Science of the total environment 482-483:214-221.

Zheng S, Wang MZ, Li B, Wang SG, He SL, Yin L, et al. 2016. Gender, Age and Season as Modifiers of the Effects of Diurnal Temperature Range on Emergency Room Admissions for Cause-Specific Cardiovascular Disease among the Elderly in Beijing. Int J Env Res Pub He 13.

Zhou XD, Zhao A, Meng X, Chen RJ, Kuang XY, Duan XL, et al. 2014. Acute effects of diurnal temperature range on mortality in 8 Chinese cities. Science of the Total Environment 493:92-97.

Appendices

Supplementary Materials

Evaluating the Effects of Temperature on Mortality in Manila City, Philippines From 2006-2010 Using Distributed Lag Nonlinear Model

---

Modeling Approach:

In the initial diagnostics, we used an NCS-NCS model with the following parameterization:

$$Log[E(Y_t)] = \alpha + \beta T_{t,l} + ns(date, 7 * 5) + ns(RHave_t, 3) + \qquad \text{(S1)}$$

$$as.factor(dow) + hod$$

Included within the initial model are variables such as the expected value of the daily counts of death (Y_t) which follows an overdispersed Poisson distribution, vector of regression coefficients for the crossbasis (β), crossbasis in pre-determined temperature and lag dimensions ($T_{t,l}$), seasonal variations (*date*), daily average relative humidity ($RHave_t$), day of the week (Downing et al.), and holiday (*hod*). Based on previous studies, we have chosen 3 degrees of freedom (df) for $RHave_t$, while 7df per year for *date* was used to control for the seasonal and long-term trends (Ishigami et al. 2008; Kaiser et al. 2002). *dow* is a factor of indicator variables and *hod* being a binary variable. We used the city's annual population as an offset to control for changes in the population size through time.

In the df-selection for lag and temperature, we created a matrix of possible combinations which ranged from 4-15df for both lag and temperature dimensions with 1df increment. Akaike Information Criterion (AIC) was used as the basis for choosing the best df combination. We have observed that 7df for temperature and 4df for lag was considered to be the best combination which has the least AIC value. In the crossbasis function, both temperature and lag were set at equally-spaced knots based on the selected df in their dimensions; temperature percentile and log values of lag, respectively. Initially, we allowed the centering of the model into default, at the mean, to determine the MMT. After few model runs, we have determined that all-cause mortality MMT was at 30°C which was located exactly at the 80th temperature percentile. We used a 15-day maximum lag period to model the effects of temperature on mortality based on previous studies (Breitner et al. 2014; Ishigami et al. 2008).

In the NCS-NCS model, based on visual inspection as well as minimum mortality determination, there are two prominent minimum points at 25.8°C and 30°C. With increased susceptibility on both extreme tails resembling that of a U-shaped pattern (Figure 1a) we further analyzed it with a Double Threshold (DTHR) model set at the thresholds; a DTHR-NCS combination. We have altered Equation S1 and tailor-fit the thresholds into Equation S2 as seen below:

$$Log[E(Y_t)] = \alpha + \beta_{Low}TLow_{t,l} + \beta_{High}THigh_{t,l} + ns(date, 7*5) + ns(RHave_t, 3) + as.factor(dow) + hod \quad \text{(S2)}$$

The initial threshold values were based on the two minimum mortality points at 25.8°C for the low threshold and 30°C for the high threshold (Figure 1b). β_{Low} and β_{High} serve as the vectors of regression coefficients for lower and higher temperature thresholds, respectively. In this study, we chose to refer to cold and heat effects as lower and higher temperature effects due to the subjectivity posed by the definition of cold and heat effects across the globe. In determining the best values for the DTHR-NCS analysis, we created combinations of multiple thresholds with 0.1°C increment for the new low threshold (lowest range value until 25.8°C) and the new high threshold (30°C until highest range value). Based on the AIC values of the multiple threshold combinations, the new low threshold was set at 23.6°C and the new high threshold was at 30.2°C. But given that the minimum temperature value in Manila City was at 23.5°C, the 0.1°C difference might not be able to capture the lower temperature effects and can be considered negligible, thus we further proceeded with a hockey-stick model with a Single High Threshold (STHR) at 30.2°C as the final model for temperature and all-cause mortality (Figure 1c).

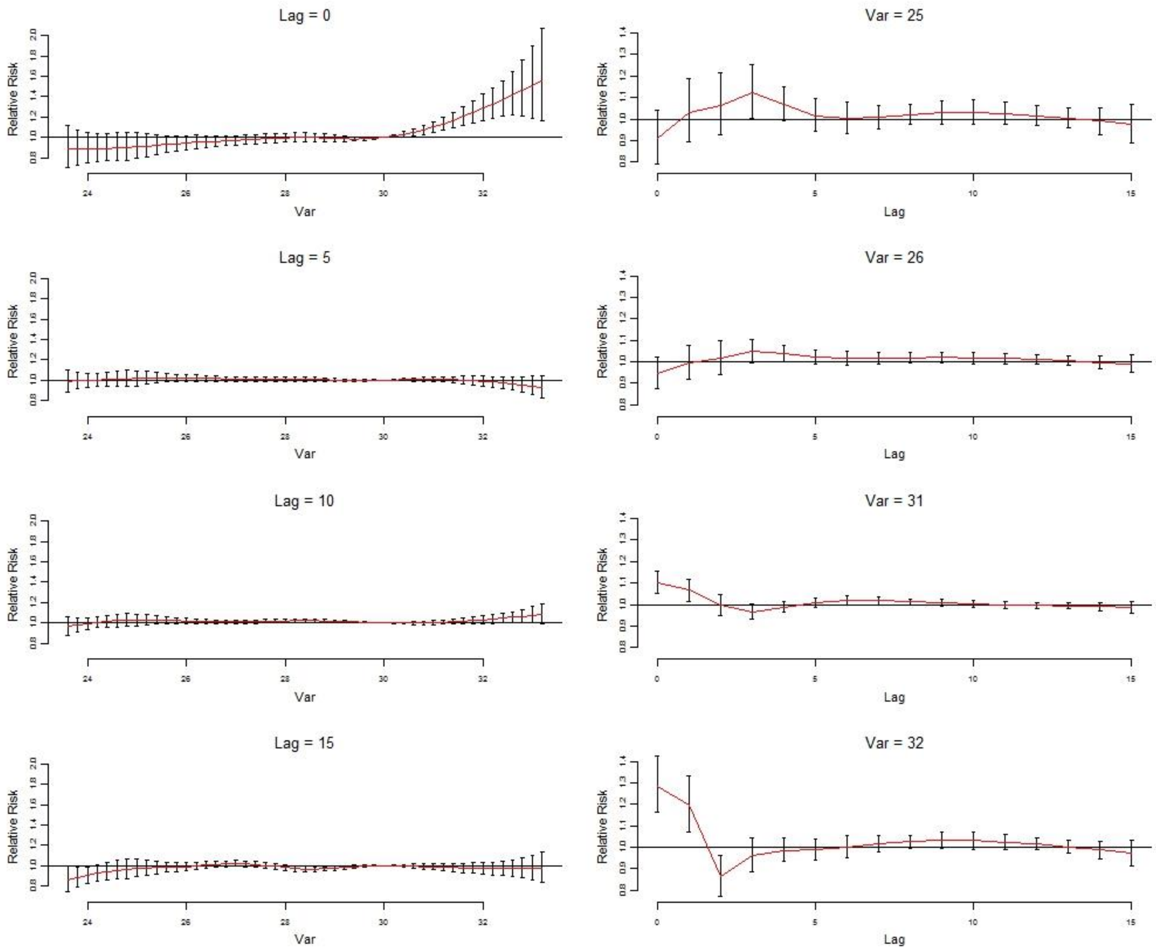

Figure S1a. Cardiovascular-causes of mortality slices in both lag (left column) and temperature dimensions (right column).

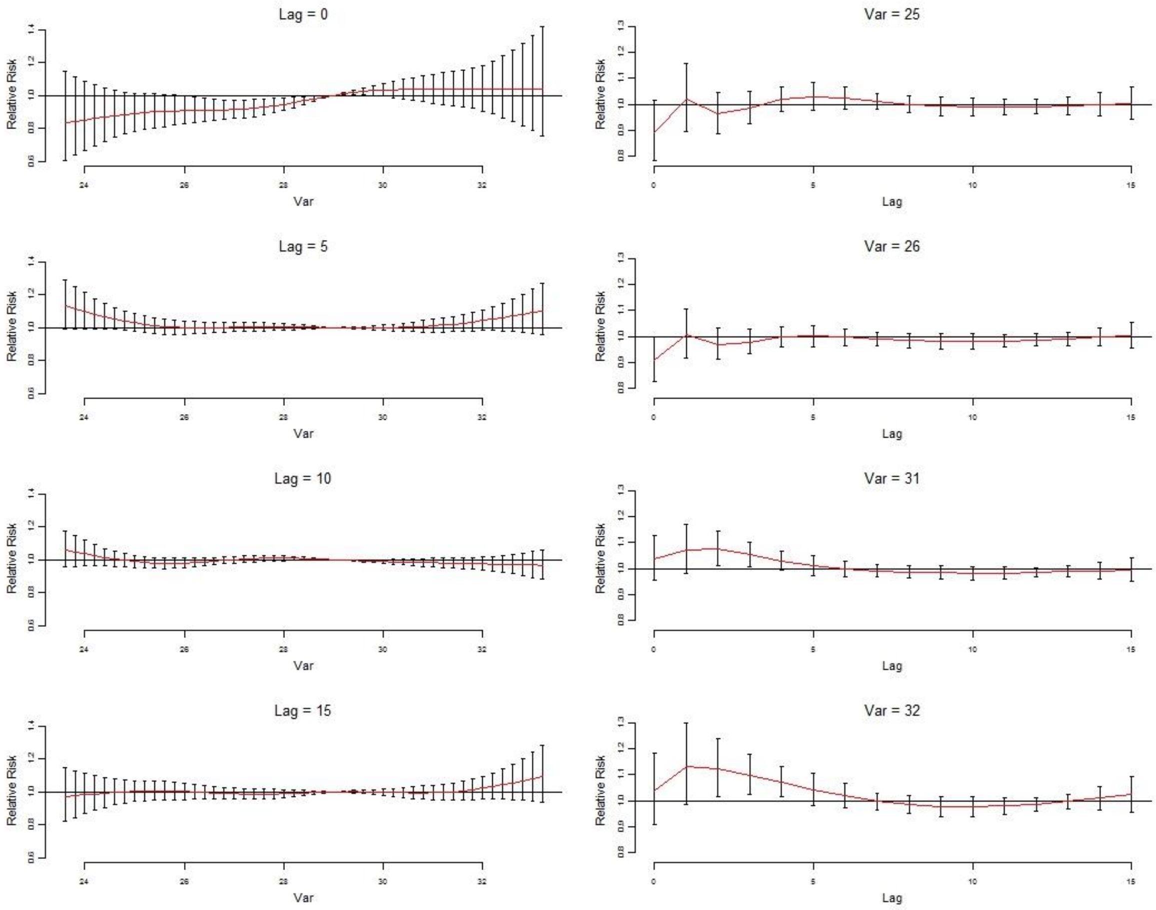

Figure S2a. Respiratory-causes of mortality slices in both lag (left column) and temperature dimensions (right column).

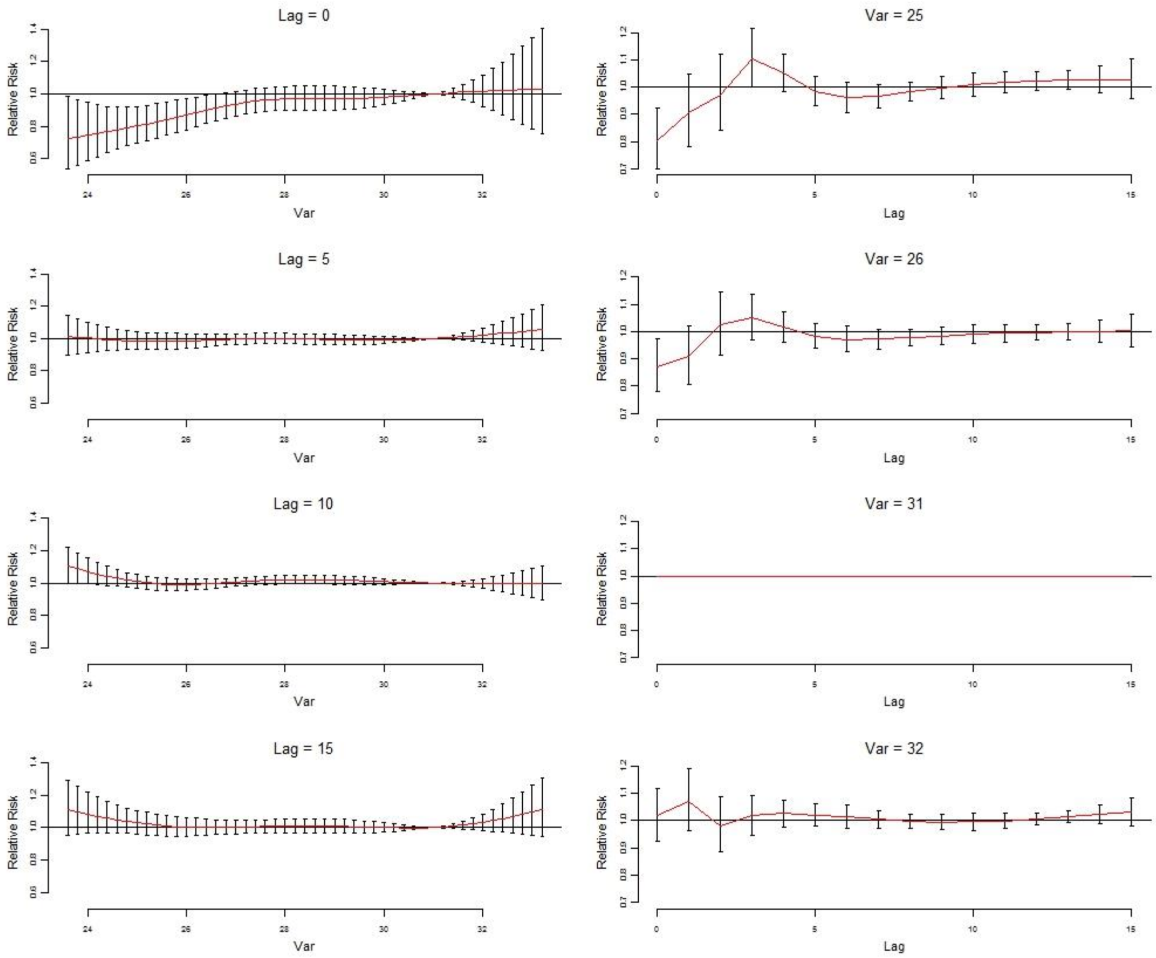

Figure S3a. 0-14y.o. mortality slices in both lag (left column) and temperature dimensions (right column).

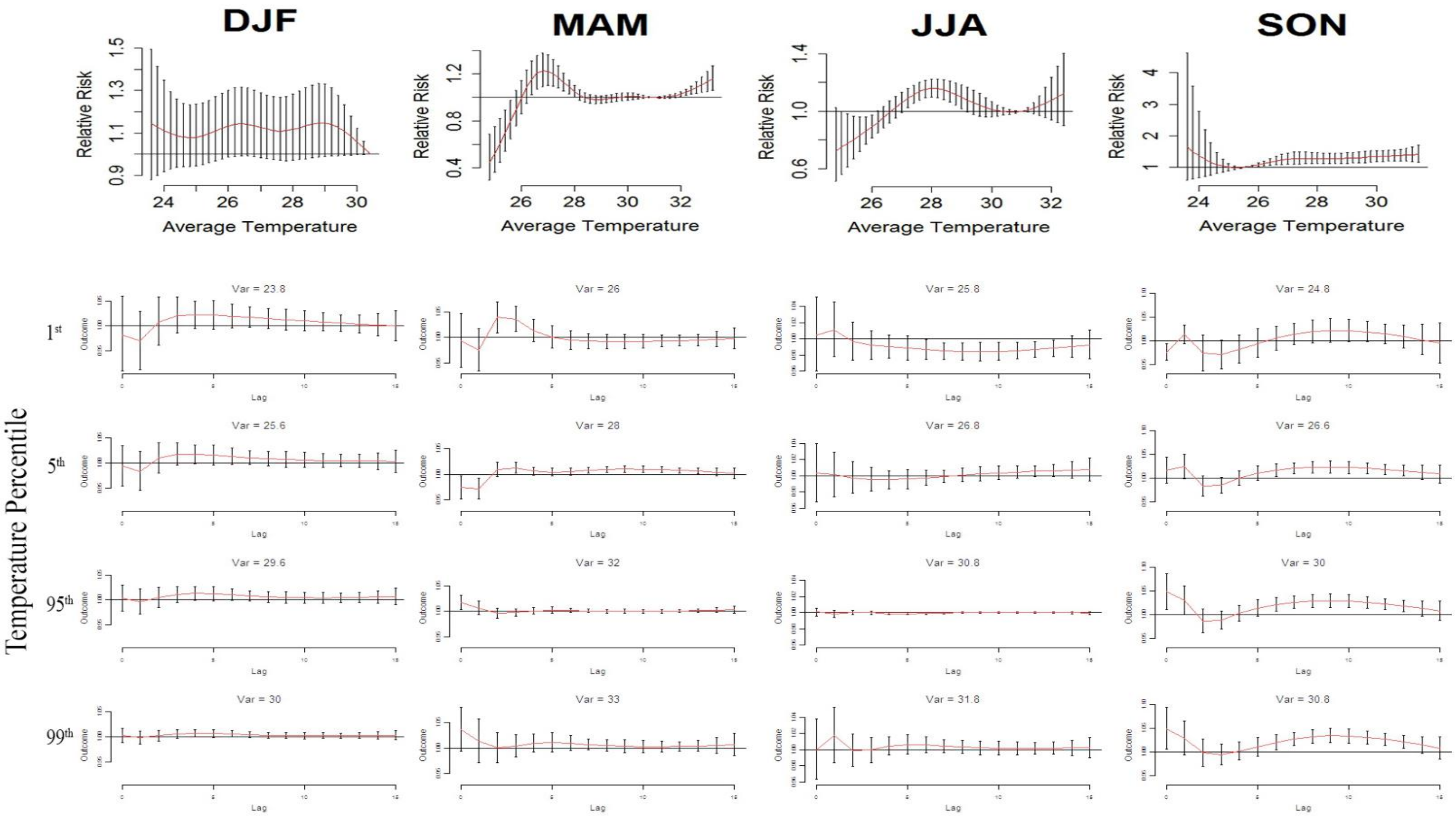

Figure S4a. Season-specific RRs with temperature-specific risks. Season-specific all-cause mortality and average temperature relationships are located in the upper most part followed by the temperature slices in their respective temperature scales; 1st, 5th, 95th, and 99th percentile, respectively.

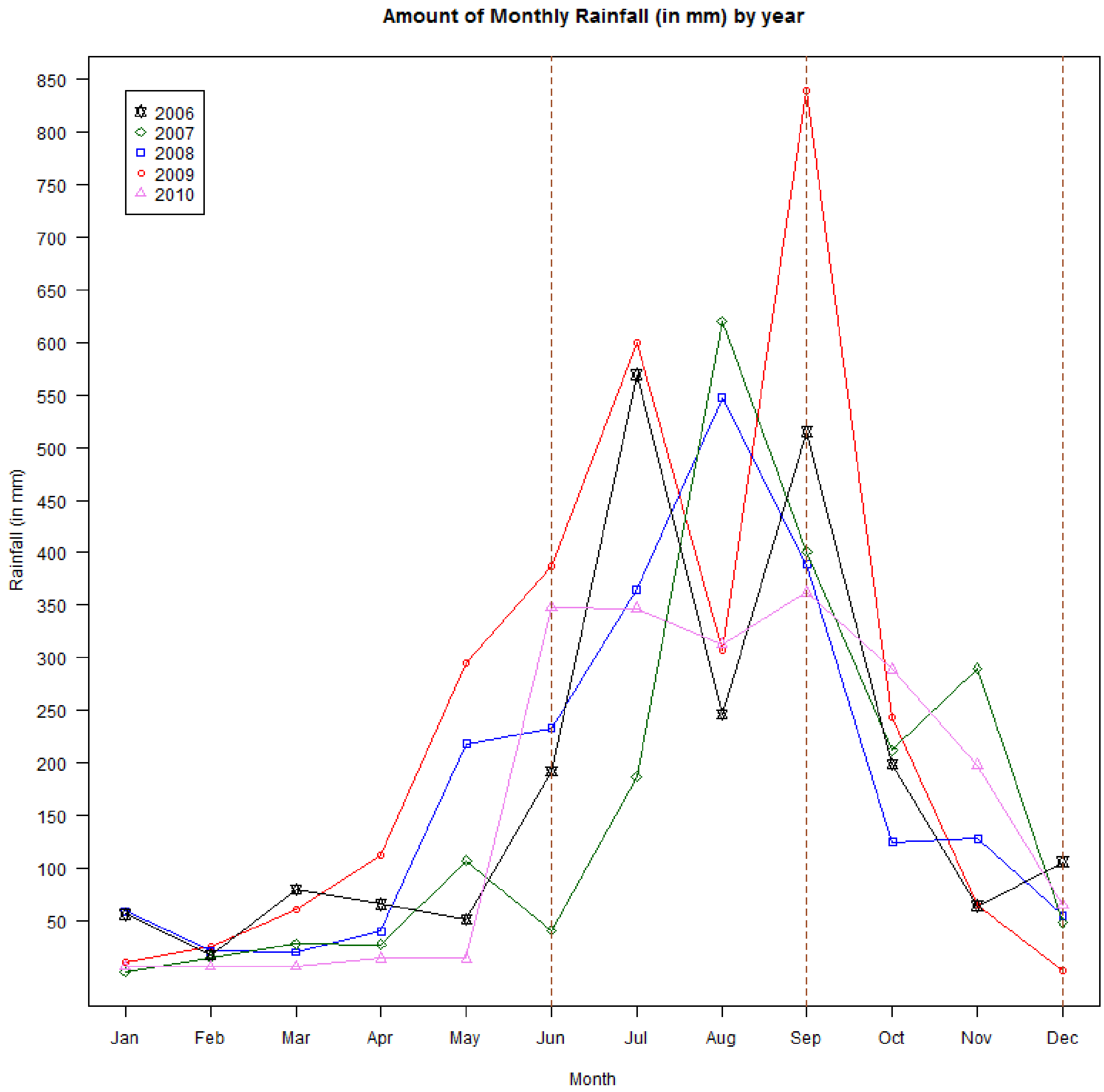

Figure S5a. Amount of Monthly Rainfall (in mm) by year in Manila City. Reference lines indicate the periods of JJA and SON seasons. Increased amount of rainfall can be observed in JJA with decreasing pattern as it continues to SON.

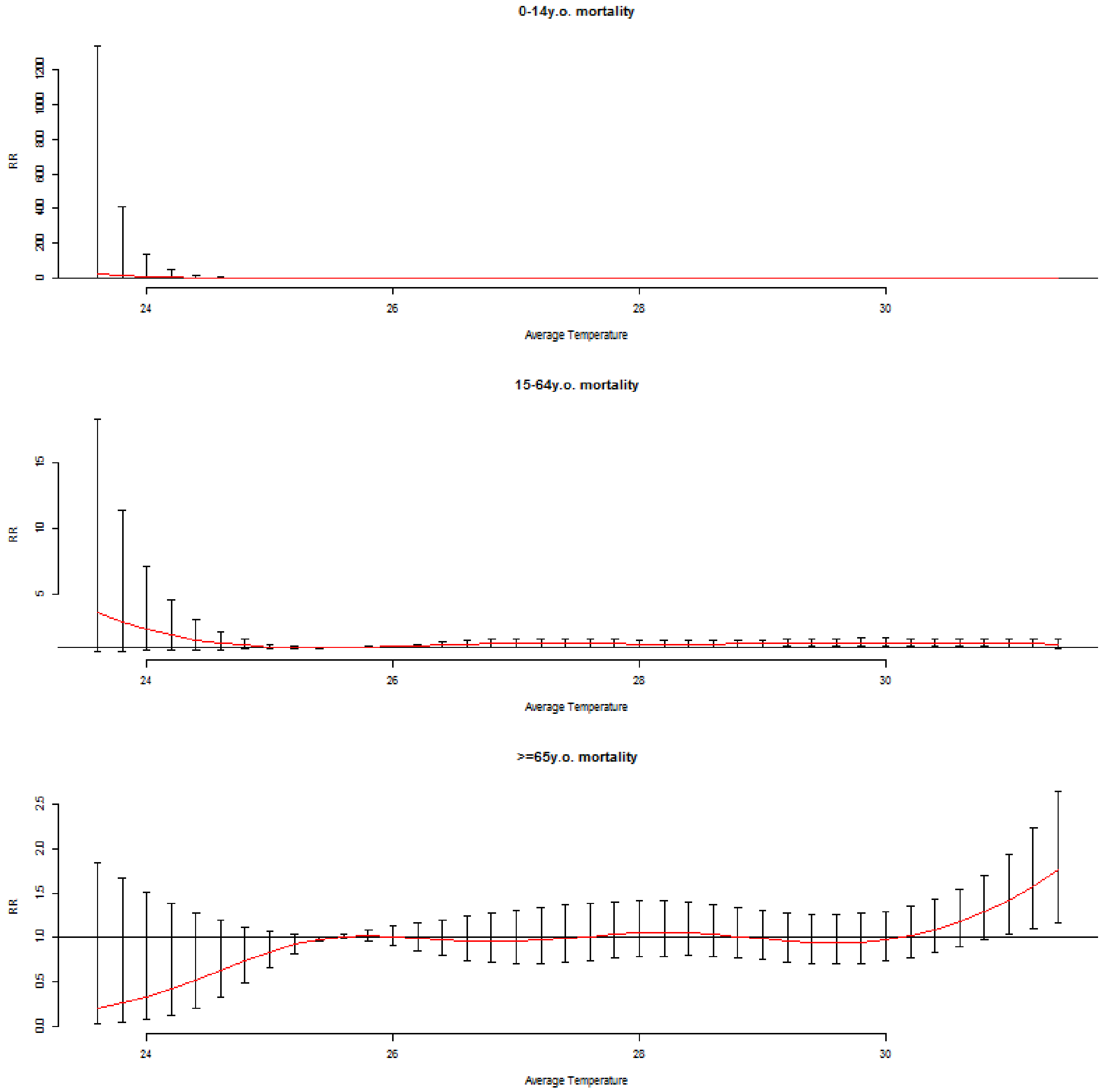

Figure S6a. SON mortality classified by age. Extremely wide confidence intervals are observed in 0-14y.o., and decreases towards >=65y.o. age group.

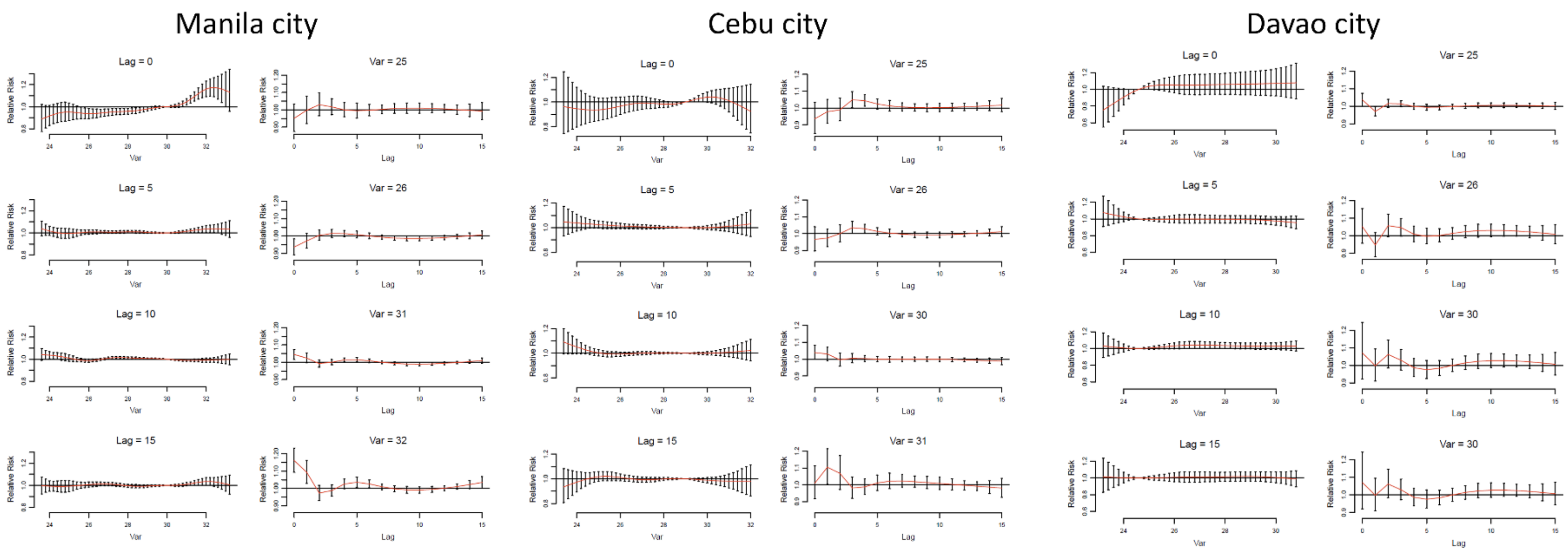

Figure S1. Dose-response slices of the three metropolitan cities on their respective lag and temperature dimensions

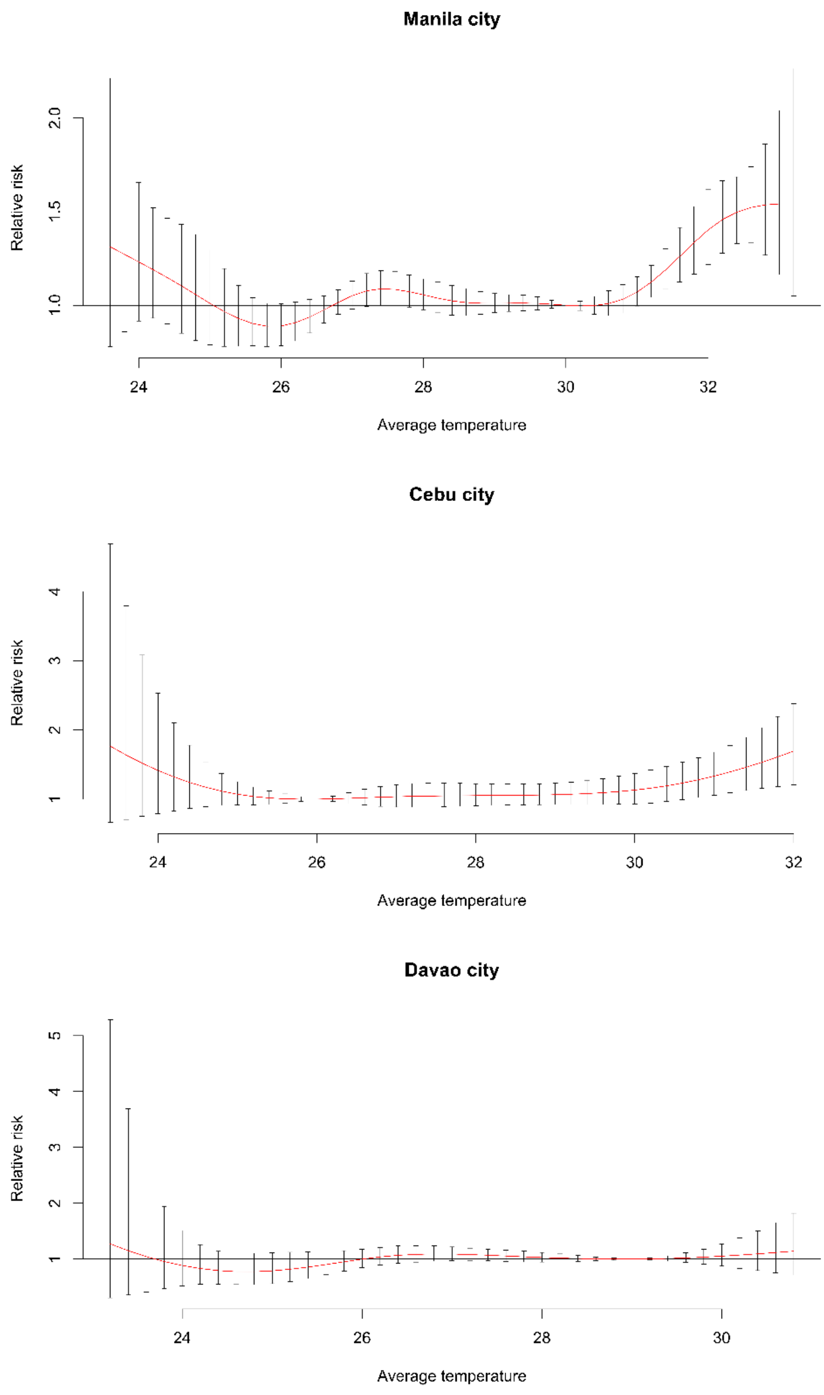

Figure S2. Overall dose-response patterns of the three metropolitan cities

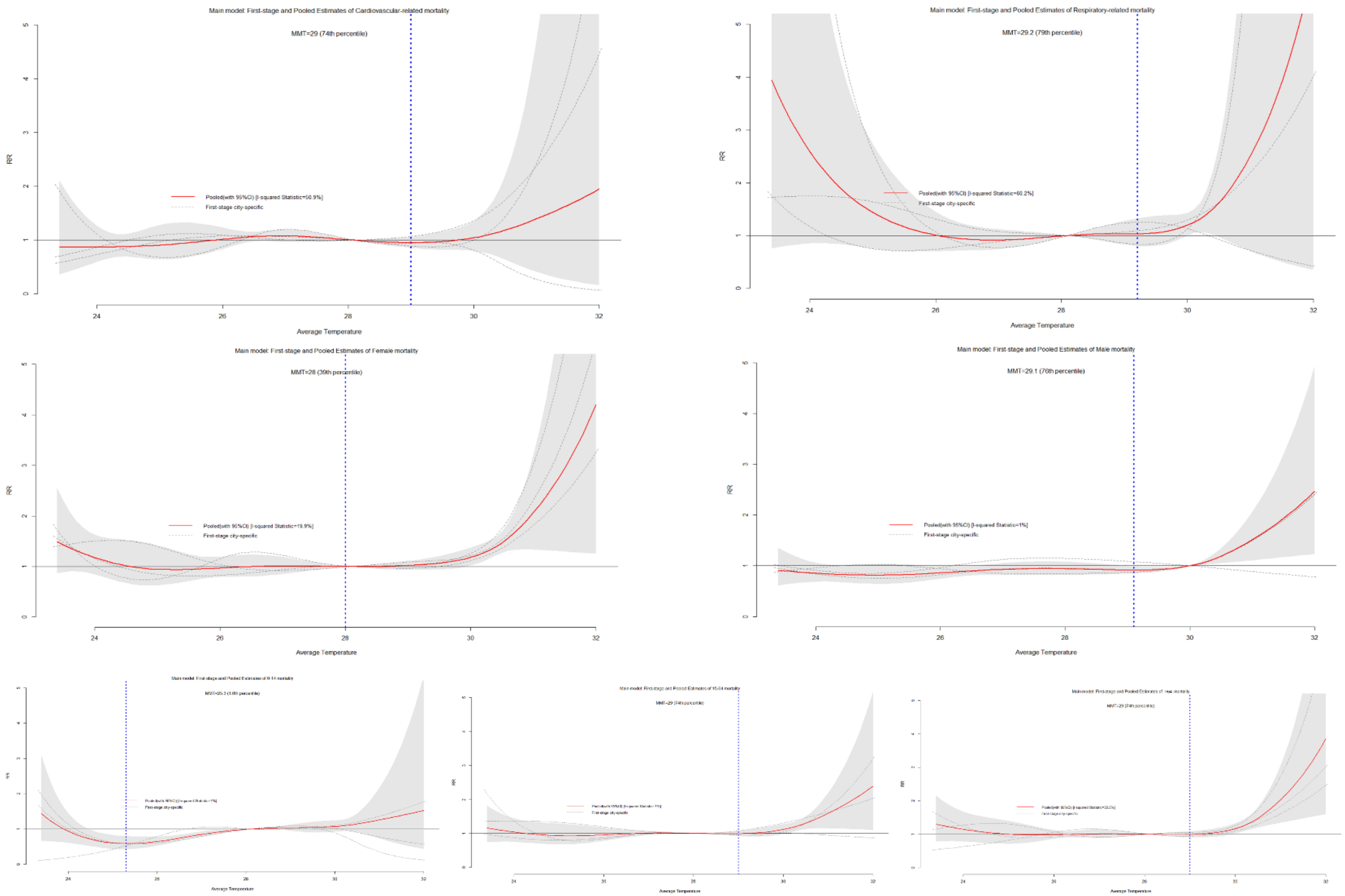

Figure S3. Meta-analytic graphs and the pooled patterns of the mortality subgroups. The dotted lines are the city-specific temperature-mortality patterns, the red solid line is the pooled pattern, and the dotted, blue vertical line is the MMT point.

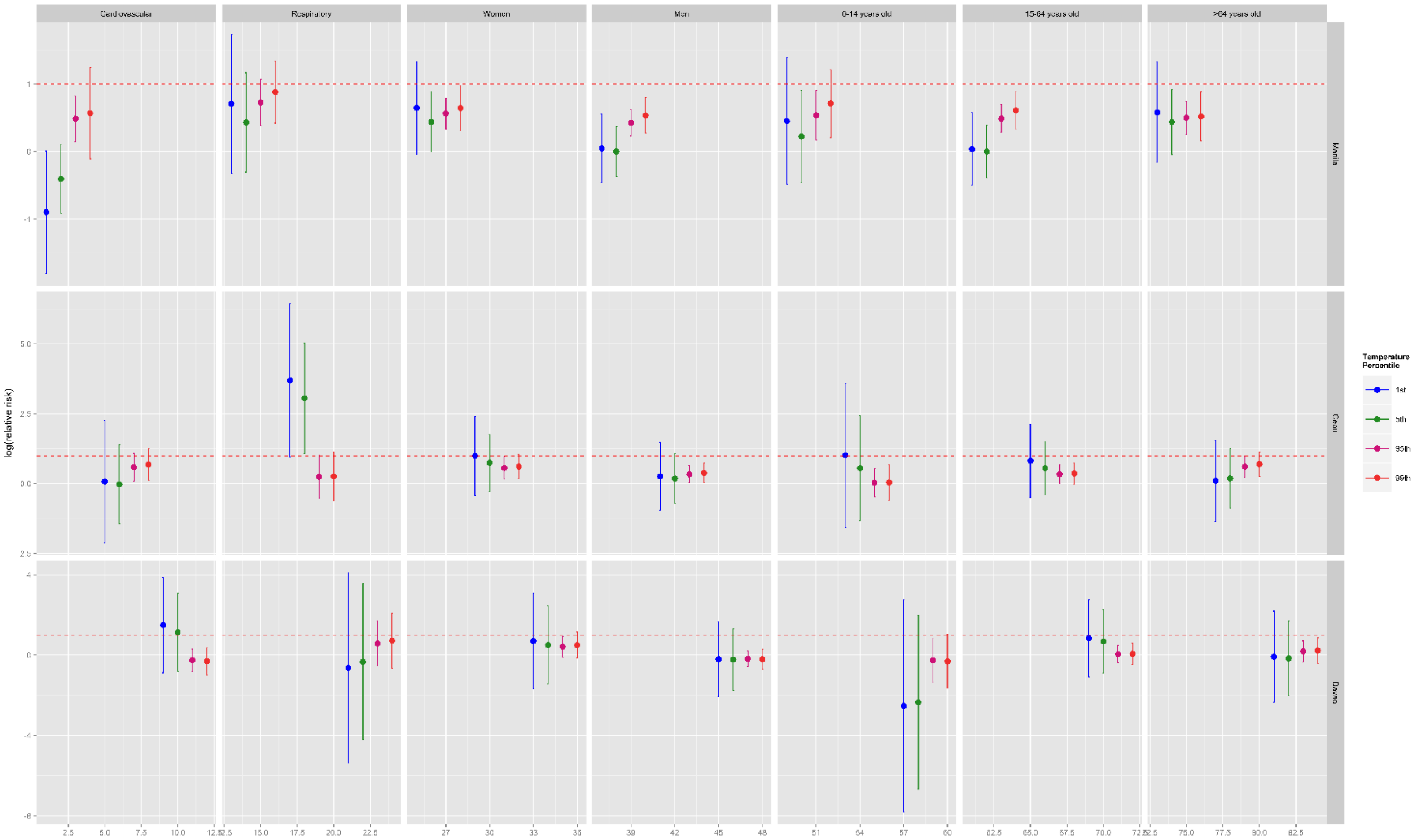

Figure S4. Individual- and city-specific log of the RR on the 1st, 5th, 95th, and 99th temperature percentiles. (We allowed free-dimensionality of the scales with respect to the temperature and log of the RR due to extremely varied RRs which masks the lower RRs.