Final Technical Report
CRRP2016-10MY-Huang

Assessing the health effects of extreme temperatures and development of adaptation strategies to climate change in the Asia-Pacific region

The following collaborators worked on this project:

1. Cunrui Huang, Sun Yat-sen University, China, huangcr@mail.sysu.edu.cn
2. Dung Phung, Griffith University, Australia, d.phung@griffith.edu.au
3. Zhiwei Xu, Queensland University of Technology, Australia, xzw1011@gmail.com
4. Wenjun Ma, Guangdong Provincial Center for Disease Control and Prevention, China, mwj68@vip.tom.com
5. Benjawan Tawatsupa, Department of Health, Ministry of Public Health, Thailand, ben_5708@hotmail.com
6. Mohammad Sohel Shomik, International Centre for Diarrhoeal Disease Research (ICDDR, B), Bangladesh, mshomik@icddrb.org
7. Do Manh Cuong, Ministry of Health of Vietnam, Vietnam, cuong_ytdp@yahoo.com
8. Cordia Chu, Griffith University, Australia, c.chu@griffith.edu.au
9. Adrian Barnett, Queensland University of Technology, Australia, a.barnett@qut.edu.au

Table of Content

Project Overview

Project Duration	:	October 2016 - March 2019
Funding Awarded	:	US$ 49,000 for Year 1; US$ 33,000 for Year 2
Key organisations involved	:	Sun Yat-Sen University, China (Prof. Cunrui Huang, Dr. Lianping Yang, Dr. Qiong Wang, Dr. Junzhe Bao) Guangdong Provincial Centre for Disease Control and Prevention, China (Prof. Wenjun Ma, Dr. Tao Liu) Ministry of Health, Vietnam (Dr. Do Manh Cuong) University of Medicine and Pharmacy in Ho Chi Minh City, Vietnam (Dr. Tran Ngoc Dang) Ministry of Public Health, Thailand (Dr. Benjawan Tawatsupa) International Centre for Diarrhoeal Disease Research, Bangladesh (Dr. Mohammad Sohel Shomik) Griffith University, Australia (Prof. Cordia Chu, Dr. Dung Phung) Queensland University of Technology, Australia (Dr. Zhiwei Xu, Prof Wenbiao Hu, Prof. Adrian Barnett)

Project Summary

Climate change is expected to be one of the biggest global health threats in the 21st century. Temperature-related health effects are the most direct and well-understood impact of climate change on human health. Most previous studies have focused on assessing mortality/morbidity in relation to extreme temperatures in high-income countries, with few studies investigating low- and middle-income countries. Countries within the Asia-Pacific region is home to more than half of the world's population, and changes in the Earth's climate are impacting human health and survival. This project aimed to quantify the health effects of extreme temperatures, particularly heat waves, in the Asia-Pacific region and to identify individual- and community-level factors which modify the health effects of temperature, attempting to formulate local adaptation strategies for dealing with heat-related health risks and reduce vulnerability. The results suggested that extreme heat events were associated with substantial burdens of morbidity/mortality in China, Vietnam and Thailand. Spatial heterogeneity in terms of heat vulnerability was also observed. The significant individual- and community-level modifiers varied across different health outcomes. The findings of this

project shed new light on the development of tailored and cost-effective climate change adaptation strategies.

Keywords：Extreme temperature, climate change; health impact, vulnerability assessment, adaptation strategy

Project outputs and outcomes

Project outputs:

- Ten publications on the health effects of temperature in China, Vietnam, and Thailand.
- One workshop and two international forums initiated by the proponent of this project (Cunrui Huang).

Project outcomes:

- Improved knowledge on the burden of diseases attributable to extreme temperatures among vulnerable populations.
- Evidence provided to decision-makers on formulating adaptation strategies to heat waves and climate change.
- Cultivated early career researchers and high degree students in the field of climate change and human health.
- Strengthened the collaborative network on climate change and health research in the Asia-Pacific region.

Key facts/figures

- Health database was built up, including work-injury claim and insurance data, ambulance dispatch data, first-ever stroke data, and also data from Birth Registry Database and Maternal and Children's Health Information System, and survey data among medical students in China, hospitalisation and death data in Vietnam, and mortality data in Thailand.
- One international workshop was held in Guangzhou, China with over 20 participants from collaborating institutes.
- Two international forums were held in Guangzhou, China with hundreds of delegates from Europe, USA, Australia, and Asian countries.

Potential for further work

- More multicity analyses and further exploration of susceptible diseases and vulnerable populations due to heat waves and climate change are needed in the Asia Pacific Region as they are densely populated.

- Based on the findings of this project, projecting the health effects of climate change in some big cities of selected countries are warranted.
- Further studies are required to understand the relative importance and interactive effects of air pollutants and temperature on health outcomes, especially in areas with high level of air pollution.
- Efforts should be taken to develop and implement adaptation strategies for alleviating public health impacts of climate change, such as heat-health warning system or real-time health surveillance system.

Publications

1. Sheng R, Li C, Wang Q, Yang L, Bao J, Wang K, et al. Does hot weather affect work-related injury? A case-crossover study in Guangzhou, China. *International Journal of Hygiene and Environmental Health* 2018;221(3):423-428.

2. Ma R, Zhong S, Morabito M, Hajat S, Xu Z, He Y, et al. Estimation of work-related injury and economic burden attributable to heat stress in Guangzhou, China. *Science of The Total Environment* 2019;666:147-154.

3. Bao J, Guo Y, Wang Q, He Y, Ma R, Hua J, et al. Effects of heat on first-ever strokes and the effect modification of atmospheric pressure: A time-series study in Shenzhen, China. *Science of The Total Environment* 2019;654:1372-1378.

4. Qiong W, Qianhong L, Changchang L, Meng R, Shao L, Luke DK, et al. Interaction of Air Pollutants and Meteorological Factors on Birth Weight in Shenzhen, China. *Epidemiology* 2019. (In press)

5. Liu T, Ren Z, Zhang Y, Feng B, Lin H, Xiao J, et al. Modification Effects of Population Expansion, Ageing, and Adaptation on Heat-Related Mortality Risks Under Different Climate Change Scenarios in Guangzhou, China. *International Journal of Environmental Research and Public Health* 2019;16(3):376.

6. Dang TN, Honda Y, Van Do D, Pham ALT, Chu C, Huang C, et al. Effects of Extreme Temperatures on Mortality and Hospitalization in Ho Chi Minh City, Vietnam. *International Journal of Environmental Research and Public Health* 2019;16(3):432.

7. Phung D, Chu C, Tran DN, Huang C. Spatial variation of heat-related morbidity: A hierarchical Bayesian analysis in multiple districts of the Mekong Delta Region. *Science of The Total Environment* 2018;637-638:1559-1565.

8. Huang C, Cheng J, Phung D, Tawatsupa B, Hu W, Xu Z. Mortality burden attributable to heatwaves in Thailand: A systematic assessment incorporating evidence-based lag structure. *Environment International* 2018;121:41-50.

9. Liao W, Yang L, Zhong S, Hess JJ, Wang Q, Bao J, et al. Preparing the next generation of health professionals to tackle climate change: Are China's medical students ready? *Environmental Research* 2019;168:270-277.

10. He Y, Ma R, Ren M, Liao W, Zhang N, Su Y, et al. Chapter 11. Public health adaptation to heat waves in response to climate change in China. *Springer* 2019. (In press).

Awards and honours

1. Lead Author for Sixth Assessment Report of IPCC Working Group II in Chapter 7: Health, wellbeing and the changing structure of communities.
2. Winner of the Australia-China Alumni Award for Science and Research in 2018.

Acknowledgements

We gratefully acknowledge the financial support provided by the Asia-Pacific Network for Global Change Research (CRRP2016-10MY-Huang). We are grateful to data providers in China, Vietnam and Thailand. We also thank all young scientists and students for their active involvements in this project. Furthermore, we acknowledge the insightful comments and contributions provided by reviewers during the journal publication procedure. Special thanks to all speakers for their valuable presentations and sharing their ideas during our international workshop and forums held in Guangzhou, China.

Chapter 1. Introduction

Because of the increasing concerns about climate change and deadly heat waves in the past, the health effects of hot weather are fast becoming a global public health challenge for the 21st century [1, 2]. A range of early impacts of climate change has been observed over recent decades, which include increasing ambient temperatures, changing precipitation patterns and an increase in the frequency of extreme weather events [3]. Temperature-related health effects are the most significant source of weather-related public health problems, also the most direct and well-understood impact of climate change on human health [4, 5]. The IPCC has stated that a future increase in heat waves will lead to excess mortality and morbidity among vulnerable populations for many regions [6].

The ability of health systems to adapt effectively to extreme temperatures and climate change is a key challenge worldwide [7]. Until now, most previous analyses have focused on mortality/morbidity in relation to heat events in high-income nations, with few studies investigating low- and middle-income countries [8]. Also, response strategies to address the health effects of temperature have not been sufficiently considered in current public health practices and activities [9]. In recognition of this challenge, it is important for countries in the Asia-Pacific region to assess the health effects of extreme temperatures, examine individual and community factors contributing to population vulnerability, then develop adaptation measures for coping with climate change.

Conceptual basis for the project

Climate change in the Asia-Pacific region. Over the past decades, human activities have released increasing quantities of carbon dioxide and other greenhouse gases (GHGs) that trap heat in the lower atmosphere, thus accelerating the rate of global warming (Figure 1). The global mean surface temperature has increased by approximately 1°C since preindustrial times, with most of that increase (0.8°C) occurring since the 1970s [3].

According to the United Nations Framework Convention on Climate Change (UNFCCC), GHG emissions are still rapidly increasing despite continued multilateral negations [11]. Atmospheric concentrations of carbon dioxide (CO_2) have risen from approximately 280 ppm in preindustrial times to 410 ppm in 2017. Meanwhile, Asia Pacific is the region with the highest rate of increase in CO_2 emissions since 1971 (Table 1).

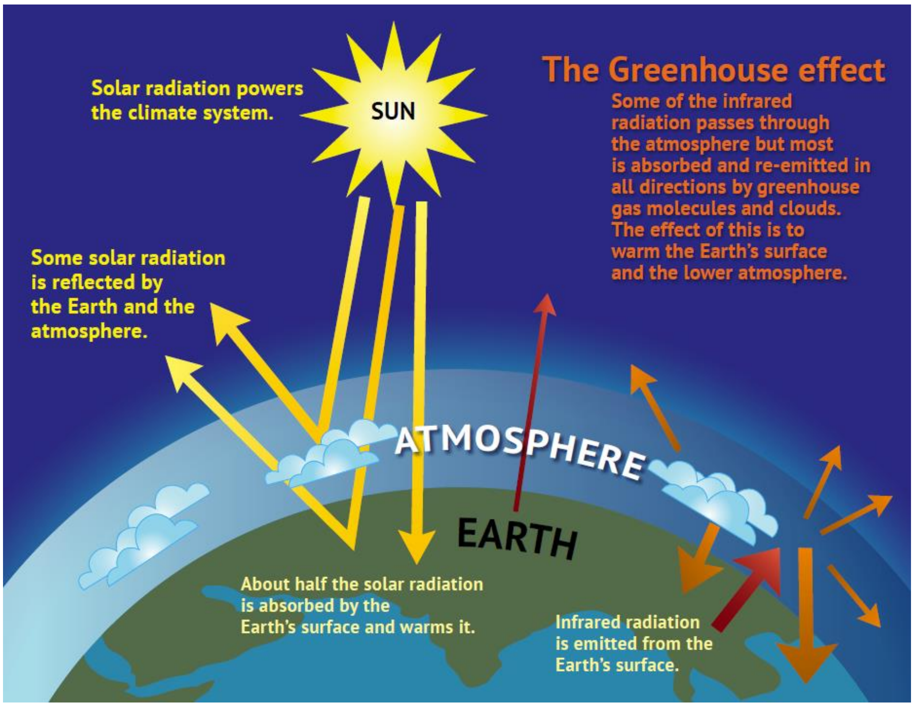


Figure 1. Illustration of the greenhouse effect. Source: [10]

Table 1. GHG emissions of selected countries in the Asia-Pacific region. Source: UNFCCC [11].

Country	GHGs emission (million tonnes of CO_2 per year)					Increase (%)			
	1971	1980	1990	2000	2010	vs 1971	vs 1980	vs 1990	vs 2000
Australia	144	208	260.0	338	383	2.7	1.8	1.5	1.1
China	800	1405	2211	3037	7217	9.0	5.1	3.3	2.4
Japan	758	880	1064	1184	1143	1.5	1.3	1.1	1.0
Korea	52	124	229	437	563	10.8	4.5	2.5	1.3
Malaysia	12	24	49	112	185	14.6	7.6	3.7	1.6
Philippines	23	33	38	67	76	3.3	2.3	2.0	1.1
Singapore	6	12	29	47	63	10.3	5.0	2.1	1.3
Viet Nam	16	14	17	44	130	8.1	8.8	7.6	3.0
World	14064	18042	20973	23509	30276	2.2	1.7	1.4	1.3

GHGs trap heat in the atmosphere, resulting in increases in the frequency, intensity and duration of extreme weather and climate events, including heat waves, floods and droughts [3]. Under climate change projections in some regions, the coolest day in the summer season by the end of this century may be warmer than the hottest day today [12]. Although the Paris Agreement was a major step forward in global efforts to tackle climate change, it would still be insufficient to limit warming to 2°C above preindustrial levels.

Table 2. Projected changes in temperature extremes in the Asia-Pacific region. Source: IPCC Fifth Assessment Report [13].

Region	Warm days	Cold days	Warm nights	Cold nights	Heat waves
Asia (excluding South-East Asia)	High confidence, likely overall increase	High confidence, likely overall decrease	High confidence, likely overall increase	High confidence, likely overall increase	Medium confidence, spatially varying trends and insufficient data in some regions High confidence, likely more areas of increase than decreases
South-East Asia and Oceania	High confidence, likely overall increase	High confidence, likely overall decrease	High confidence, likely overall increase	High confidence, likely overall decrease	Low confidence (due to lack of literature) to high confidence depending on region High confidence, likely overall increase in Australia

The health impacts of climate change. Scientific evidence has clearly shown the adverse impacts of climate change on human health. Figure 2 summarizes the health risks that could be associated with climate change [14]. Major pathways through which climate change affects health may include direct impacts, such as extra deaths due to heat waves; impacts mediated through natural systems, such as effects on vector-borne diseases; and impacts mediated through socioeconomic systems, such as mental health problems caused by income loss resulting from a reduction in agricultural productivity associated with floods, droughts and other extremes [12].

The World Health Organization (WHO) estimated that approximately 250,000 deaths annually between 2030 and 2050 could be due to climate change-related increases in heat exposure in the elderly, as well as increases in diarrheal disease, dengue fever, malnutrition and mental illness [15]. The magnitude of disease burden depends not just on the hazards posed by climate change but also on the sensitivity of the populations that are exposed to those hazards and on the capacity of infrastructure and health systems to manage the risks [12, 16].

Health risks associated with heat waves. Heatwave commonly refers to an extended period of unusually hot weather, but it seems that there is no simple definition. In general, magnitude, duration and frequency are essential to constitute a heat wave, but the definition varies depending on the meteorological variables or health outcomes of interest. One debatable issue exists concerning definitions based on absolute temperatures versus percentiles. Absolute temperatures are important for human biophysical heat tolerances, but percentiles may be comparable across different areas and time scales given differences in acclimatization and preparedness [17]. Another issue arises because of the strong association between humidity and thermal stress in humans. Thus, 'apparent temperature' or 'humidex' [18], which combines temperature and humidity, is also a choice to define heat waves.

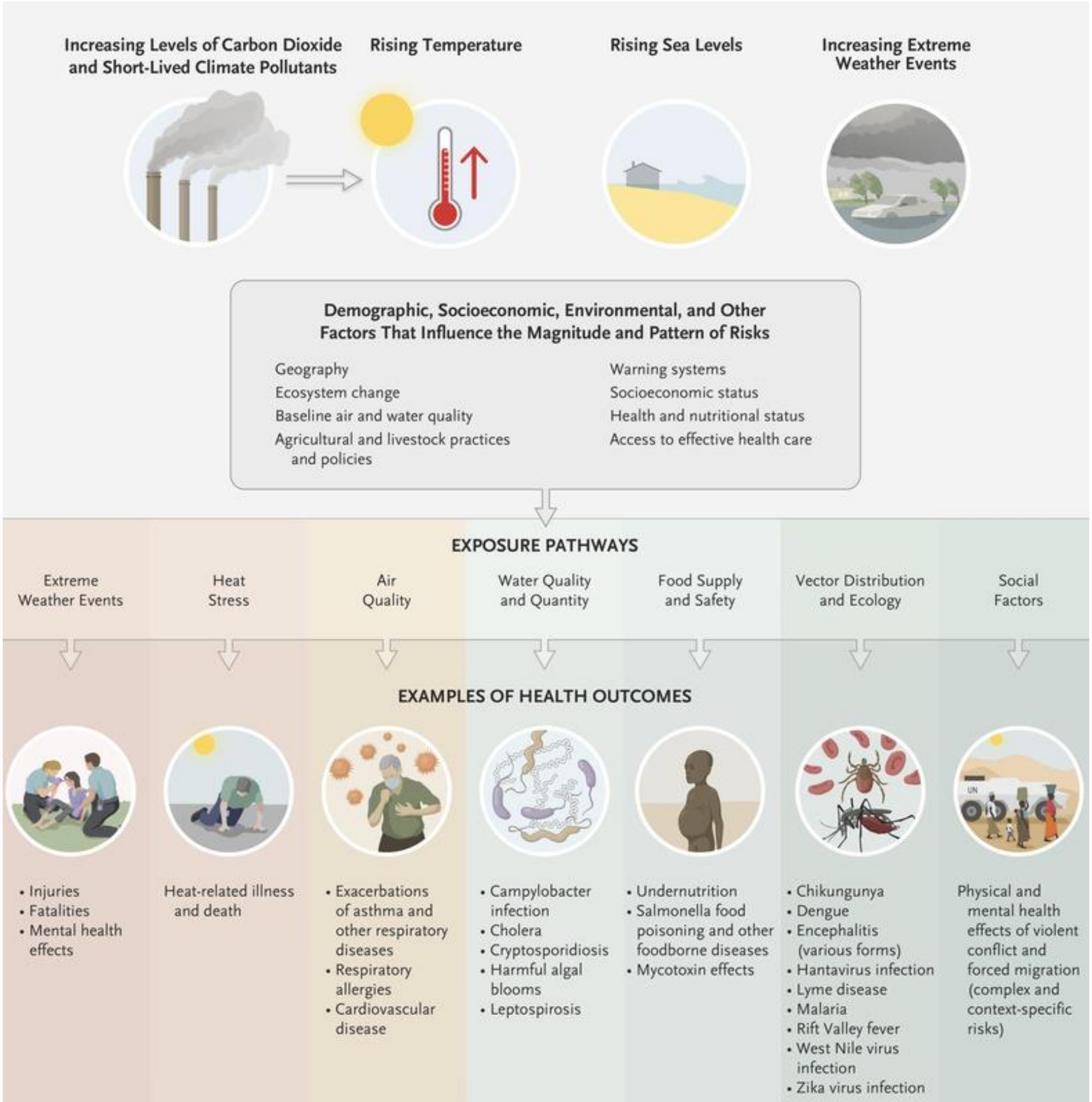


Figure 2. The adverse health impacts of climate change. Source: [14]

Heat waves can cause a wide range of health problems (Figure 3). A rise of 1 °C above the local unusually hot threshold may account for 1-3% increase in all-cause mortality [19, 20]. The increased mortality is mainly attributed to the cardio-cerebrovascular system, central nervous system and respiratory system, which are highly sensitive to heat [21, 22]. Compared with mortality, heat-related morbidity is less well studied for that death data are easier to access around the world [23]. Research so far has also shown inconsistent findings on morbidity. For example, during heat waves, increased in ischemic heart disease and stroke were found in California [24] while the rising number of respiratory and renal diseases were illustrated in London [25]. In general, the rising number of emergency hospitalization are mostly attributed to heat-related illnesses, such as heat stroke, dehydration and electrolyte disturbances, as well as pre-existing diseases with other International Classification of Diseases (ICD) chapters but actually related with heat, such as cardio-cerebrovascular diseases, respiratory illness, chronic renal diseases, reduced function of central nervous, and mental disorders [21].

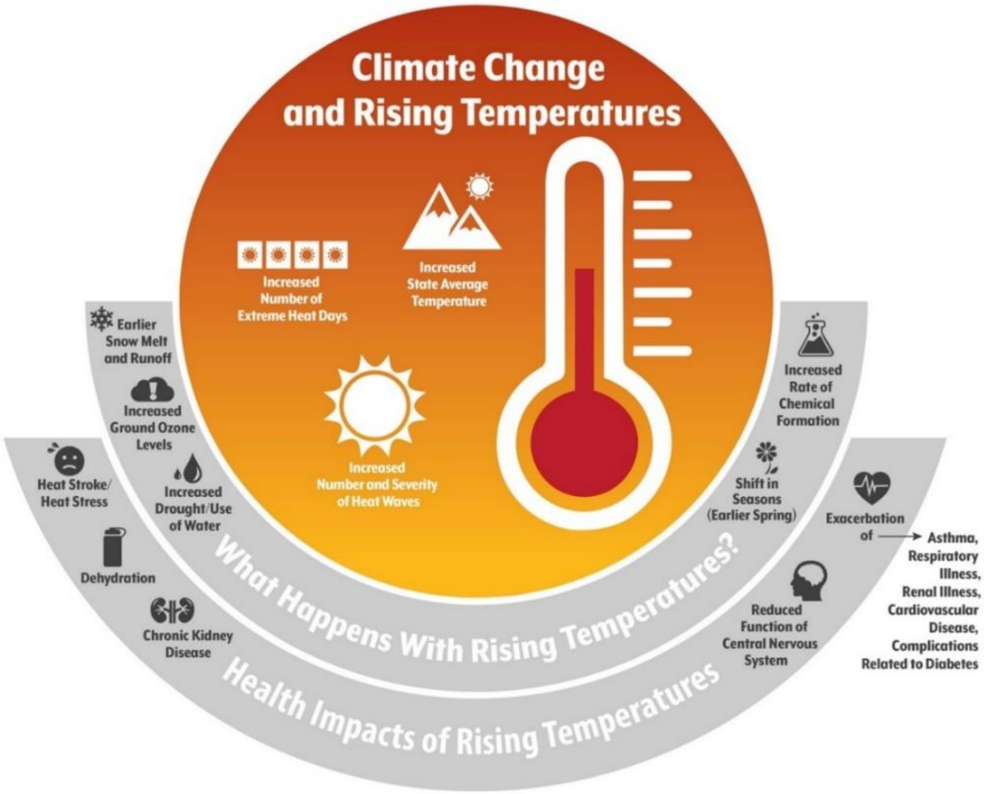


Figure 3. Rising temperature and its health impacts. Source: [26].

The aims of this APN project. Climate change is expected to be one of the biggest global health threats in this century [27]. Public health adaptation is inevitably required to address the adverse health impacts of climate change over the next few decades. Countries within the Asia-Pacific region is home to more than half of the world's population, and changes in the Earth's climate are impacting the societies, economies and survivals of humans. With unique geographies and population groups, the Asia-Pacific region is exceptionally diverse, including the least developed countries, rapidly-emerging economies and developed nations. This diversity is reflected in climate change and health risks that vary considerably from one environment to another.

Although researchers have been investigating the implications of a changing climate for sensitive health outcomes; partly because of limited funding, the evidence base remains fragmented and limited. Therefore, if we are to manage the health risks of climate change, we must work together to take science-informed action. The Asia-Pacific Network for Global Change Research (APN) is a network of member country governments that promotes global change research in the region that has potential, in addition to improving the understanding of climate change and its risks in the region, to contribute to the development of science-based response strategies to address these challenges.

With the scientific and financial support from APN, our research team have endeavoured to investigate the health effects of extreme temperatures and climate change in the Asia-Pacific region and to formulate local adaptation strategies for dealing with heat-related health risks and reduce vulnerability. In this report, we provide sound evidence on the health effects of extreme temperatures in the context of climate change from selected countries in the Asia-Pacific region. It also offers research directions and policy suggestions for future action in the region. The research will have the potential to make a significant contribution to protecting the health of present and future generations in the Asia-Pacific region.

The outline of the final report

The final report is presented in a publication style. As such, each body section is designed to stand alone. Chapter 2 is to bring together quantitative assessments of temperature-related health effects in the Asia Pacific region from selected countries including China, Vietnam and Thailand.

Section 2.1 investigates the association between high temperatures and work-related injuries. This study reveals a higher risk of work-related injuries due to hot weather in Guangzhou, China. Significant associations were seen for both males and females, and middle-aged workers, and those working in manufacturing, transport and construction sectors.

Section 2.2 quantifies the attributable fractions of work-related injury claims and subsequent insurance payouts in Guangzhou, China. Results indicate that heat stress can contribute to a higher risk of work-related injury and substantial economic costs. Male workers, those in small enterprises and with low educational attainment were especially sensitive to the effects of heat exposure.

Section 2.3 investigates the heat impacts on ambulance dispatches in Shenzhen, China. Significantly rising risks and wider range of heat-related diseases compared to mortality or hospitalization data were reported. Susceptible diseases were urinary disease, alcohol intoxication, obstetric and gynaecological disease, dizziness, respiratory disease, traumatic disease, and gastrointestinal disease.

Section 2.4 evaluates the effects of heat on first-ever strokes, the possible sensitive populations, and the effect of modification of atmospheric pressure in Shenzhen, China. Results suggest that high temperatures in hot months may trigger first-ever strokes, and low atmospheric pressure may exacerbate the effect.

Section 2.5 assesses the interaction effects of meteorological factors and air pollutants on birth outcomes in Shenzhen, China. This research observes interactive effects of both air temperature and humidity on PM_{10} and small for gestational age for newborns conceived in the warm season (May– October).

Section 2.6 conducts a comprehensive study to quantify the heat-related years of life lost (YLLs) of future warming climate under the RCP scenarios on a local scale in China. Results show that heat effects may increase dramatically with continued rapid population expansion processes and population ageing in the future.

Section 2.7 examines the effects of extreme heat events on mortality and hospitalization in Ho Chi Minh City, the most populous city of Vietnam. The effect of heat waves significantly increased the risk of all cause-specific mortality and hospitalization for respiratory diseases.

Section 2.8 investigates spatial variability of heat-related morbidity in multiple districts of the Mekong Delta Region, Vietnam. Heterogeneous of temperature-hospitalization risks were found across districts. Population density, per cent of females, pre-school students and rural population in districts could lead to this heterogeneity.

Section 2.9 quantifies the acute and cumulative effects of heat waves on mortality in Thailand. This study reveals the highest risks of deaths from certain infectious and parasitic diseases and neoplasms during heat wave, causing considerable mortality burden.

Section 2.10 assesses the current medical students' perception and capacity in response to climate change in China. Results suggest that medical students in China were aware of climate change and felt responsible, but they were not ready to make responses to its health impacts. Educational efforts should reinforce eco-medical literacy development and capacity building in the era of climate change.

Chapter 3 examines heat-related health effects and suggests public health adaptation strategies to extreme heat events in the Asia-Pacific region. The chapter has identified several adaptation strategies to address the health impacts of heat waves and discussed the issues of implementing these policies and measures.

References

1. Hajat, S.; O'Connor, M.; Kosatsky, T., Health effects of hot weather: from awareness of risk factors to effective health protection. Lancet 2010, 375, (9717), 856-863.
2. Watts, N.; Amann, M.; Ayeb-Karlsson, S.; Belesova, K.; Bouley, T.; Boykoff, M.; Byass, P.; Cai, W.; Campbell-Lendrum, D.; Chambers, J.; Cox, P. M.; Daly, M.; Dasandi, N.; Davies, M.; Depledge, M.; Depoux, A.; Dominguez-Salas, P.; Drummond, P.; Ekins, P.; Flahault, A.; Frumkin, H.; Georgeson, L.; Ghanei, M.; Grace, D.; Graham, H.; Grojsman, R.; Haines, A.; Hamilton, I.; Hartinger, S.; Johnson, A.; Kelman, I.; Kiesewetter, G.; Kniveton, D.; Liang, L.; Lott, M.; Lowe, R.; Mace, G.; Odhiambo Sewe, M.; Maslin, M.; Mikhaylov, S.; Milner, J.; Latifi, A. M.; Moradi-Lakeh, M.; Morrissey, K.; Murray, K.; Neville, T.; Nilsson, M.; Oreszczyn, T.; Owfi, F.; Pencheon, D.; Pye, S.; Rabbaniha, M.; Robinson, E.; Rocklöv, J.; Schütte, S.; Shumake-Guillemot, J.; Steinbach, R.; Tabatabaei, M.; Wheeler, N.; Wilkinson, P.; Gong, P.; Montgomery, H.; Costello, A., The Lancet Countdown on health and climate change: from 25 years of inaction to a global transformation for public health. The Lancet 2017.
3. IPCC, Climate Change 2013: The Physical Science Basis. 2013.
4. Kinney, P. L., Health: A new measure of health effects. Nature Clim. Change 2012, 2, (4), 233-234.
5. Huang, C.; Barnett, A. G.; Wang, X.; Tong, S., The impact of temperature on years of life lost in Brisbane, Australia. Nature Clim Change 2012, 2, (4), 265-270.
6. IPCC, Climate change 2014–Impacts, adaptation and vulnerability: Regional aspects. Cambridge University Press: 2014.
7. McGregor, G. R.; Vanos, J. K., Heat: a primer for public health researchers. Public Health 2018, 161, 138-146.
8. Benmarhnia, T.; Deguen, S.; Kaufman, J. S.; Smargiassi, A., Vulnerability to Heat-related Mortality: A Systematic Review, Meta-analysis, and Meta-regression Analysis. Epidemiology 2015, 26, (6), 781-793.
9. Huang, C.; Barnett, A. G.; Xu, Z.; Chu, C.; Wang, X.; Turner, L. R.; Tong, S., Managing the health effects of temperature in response to climate change: challenges ahead. Environ Health Perspect 2013, 121, (4), 415-419.
10. IPCC, Climate change 2007-the physical science basis: Working group I contribution to the fourth assessment report of the IPCC. Cambridge university press: 2007; Vol. 4.
11. UNFCC, GHG data - UNFCCC. In 2013.
12. Haines, A.; Ebi, K., The Imperative for Climate Action to Protect Health. New England Journal of Medicine 2019, 380, (3), 263-273.
13. IPCC, Climate change 2013: the physical science basis. Contribution of Working Group I to the fifth assessment report of the Intergovernmental Panel on Climate Change. Cambridge University Press: Cambridge and New York, 2013.
14. Haines, A.; Ebi, K., The Imperative for Climate Action to Protect Health. N Engl J Med 2019, 380, (3), 263-273.
15. WHO, Quantitative risk assessment of the effects of climate change on selected causes of death, 2030s and 2050s. World Health Organization: 2014.
16. Huang, C.; Vaneckova, P.; Wang, X.; FitzGerald, G.; Guo, Y.; Tong, S., Constraints and barriers to public health adaptation to climate change: a review of the literature. Am J Prev Med 2011, 40, (2), 183-190.
17. Horton, R. M.; Mankin, J. S.; Lesk, C.; Coffel, E.; Raymond, C., A Review of Recent Advances in Research on Extreme Heat Events. Current Climate Change Reports 2016, 2, (4), 242-259.
18. Steadman, R. G., A Universal Scale of Apparent Temperature. Journal of Climate and Applied Meteorology 1984, 23, (12), 1674-1687.

19. Gasparrini, A.; Guo, Y.; Hashizume, M.; Lavigne, E.; Zanobetti, A.; Schwartz, J.; Tobias, A.; Tong, S.; Rocklöv, J.; Forsberg, B.; Leone, M.; De Sario, M.; Bell, M. L.; Guo, Y.-L. L.; Wu, C.-f.; Kan, H.; Yi, S.-M.; de Sousa Zanotti Stagliorio Coelho, M.; Saldiva, P. H. N.; Honda, Y.; Kim, H.; Armstrong, B., Mortality risk attributable to high and low ambient temperature: a multicountry observational study. The Lancet 2015, 386, (9991), 369-375.
20. Margolis, H. G., Heat Waves and Rising Temperatures: Human Health Impacts and the Determinants of Vulnerability. In Global Climate Change and Public Health, Pinkerton, K. E.; Rom, W. N., Eds. Springer New York: New York, NY, 2014; pp 85-120.
21. Kravchenko, J.; Abernethy, A. P.; Fawzy, M.; Lyerly, H. K., Minimization of heatwave morbidity and mortality. Am J Prev Med 2013, 44, (3), 274-82.
22. Huang, C.; Barnett, A. G.; Wang, X.; Tong, S., Effects of extreme temperatures on years of life lost for cardiovascular deaths: a time series study in Brisbane, Australia. Circulation. Cardiovascular quality and outcomes 2012, 5, (5), 609-14.
23. Li, M.; Gu, S.; Bi, P.; Yang, J.; Liu, Q., Heat waves and morbidity: current knowledge and further direction-a comprehensive literature review. Int J Environ Res Public Health 2015, 12, (5), 5256-83.
24. Basu, R.; Pearson, D.; Malig, B.; Broadwin, R.; Green, R., The effect of high ambient temperature on emergency room visits. Epidemiology 2012, 23, (6), 813-20.
25. Kovats, R. S.; Hajat, S.; Wilkinson, P., Contrasting patterns of mortality and hospital admissions during hot weather and heat waves in Greater London, UK. Occup Environ Med 2004, 61, (11), 893-8.
26. Maggie Bailey; Chrissy Esposito; Brian Clark; Foster, C.; Goeken, D.; Hanel, J.; Johnson, E.; Schmitt, S. Colorado's Climate and Colorado's Health Examining the Connection; Courtesy of the Colorado Health Institute: July 10, 2017, 2017.
27. Watts, N.; Adger, W. N.; Agnolucci, P.; Blackstock, J.; Byass, P.; Cai, W.; Chaytor, S.; Colbourn, T.; Collins, M.; Cooper, A.; Cox, P. M.; Depledge, J.; Drummond, P.; Ekins, P.; Galaz, V.; Grace, D.; Graham, H.; Grubb, M.; Haines, A.; Hamilton, I.; Hunter, A.; Jiang, X.; Li, M.; Kelman, I.; Liang, L.; Lott, M.; Lowe, R.; Luo, Y.; Mace, G.; Maslin, M.; Nilsson, M.; Oreszczyn, T.; Pye, S.; Quinn, T.; Svensdotter, M.; Venevsky, S.; Warner, K.; Xu, B.; Yang, J.; Yin, Y.; Yu, C.; Zhang, Q.; Gong, P.; Montgomery, H.; Costello, A., Health and climate change: policy responses to protect public health. The Lancet 2015, (0).

Chapter 2. Synthesis of climate change and health research in the Asia-Pacific Region

This chapter is to bring together quantitative assessments of temperature-related health effects in the Asia Pacific region from selected countries including China, Vietnam and Thailand.

Section 2.1 investigates the association between high temperatures and work-related injuries in Guangzhou, China. Section 2.2 quantifies the attributable fractions of work-related injury claims and subsequent insurance payouts due to heat stress in Guangzhou, China. Section 2.3 investigates the heat impacts on ambulance dispatches in Shenzhen, China. Section 2.4 evaluates the effects of heat on first-ever strokes, the possible sensitive populations, and the effect of modification of atmospheric pressure in Shenzhen, China. Section 2.5 assesses the interaction effects of meteorological factors and air pollutants on birth outcomes in Shenzhen, China. Section 2.6 conducts a comprehensive study to quantify the heat-related years of life lost of future warming climate under the RCP scenarios on a local scale in China. Section 2.7 examines the effects of extreme heat events on mortality and hospitalization in Ho Chi Minh City, the most populous city of Vietnam. Section 2.8 investigates spatial variability of heat-related morbidity in multiple districts of the Mekong Delta Region, Vietnam. Section 2.9 quantifies the acute and cumulative effects of heat waves on mortality in Thailand. Section 2.10 assesses the current medical students' perception and capacity in response to climate change in China.

2.1 Does hot weather affect work-related injury? a case-crossover study in Guangzhou, China

Rongrong Sheng [1,#], Changchang Li [1,#], Qiong Wang [1], Lianping Yang [1], Junzhe Bao [1], Kaiwen Wang [1], Rui Ma [1], Chuansi Gao [2], Shao Lin [3], Ying Zhang [4], Peng Bi [5], Chuandong Fu [6,*], Cunrui Huang [1,*]

[1] School of Public Health, Sun Yat-sen University, Guangzhou, China

[2] Thermal Environment Laboratory, Division of Ergonomics and Aerosol Technology, Department of Design Sciences, Faculty of Engineering, Lund University, Lund, Sweden

[3] Departments of Environmental Health Sciences and Epidemiology and Biostatistics, University at Albany, State University of New York, Rensselaer, NY, USA

[4] School of Public Health, The University of Sydney, Sydney, New South Wales, Australia

[5] Discipline of Public Health, The University of Adelaide, Adelaide, Australia

[6] Guangdong Province Work Injury Rehabilitation Hospital, Guangzhou, China

[#] First Authors

[*] Correspondence: huangcr@mail.sysu.edu.cn (C.H.); fucd168168@163.com (C.F.)

Sheng R, Li C, Wang Q, Yang L, Bao J, Wang K, et al. Does hot weather affect work-related injury? A case-crossover study in Guangzhou, China. International Journal of Hygiene and Environmental Health 2018;221(3):423-428.

Abstract:

Background: Despite increasing concerns about the health effects of climate change, the extent to which workers are affected by hot weather is not well documented. This study aims to investigate the association between high temperatures and work-related injuries using data from a large subtropical city in China.

Methods: We used workers' compensation claims to identify work-related injuries in Guangzhou, China during 2011–2012. To feature the heat effect, the study period was restricted to the warm seasons in Guangzhou (1 May-31 October). We conducted a time-stratified case-crossover study to examine the association between ambient outdoor temperatures, including daily maximum and minimum temperatures, and cases of work-related injury. The relationships were assessed using conditional Poisson regression models.

Results: Overall, a total of 5,418 workers' compensation claims were included in the study period. Both maximum and minimum temperature were significantly associated with work-related injuries, but associations varied by subgroup. 1 °C increase in maximum temperature was associated with a 1.4% (RR=1.014, 95%CIs 1.012-1.017) increase in daily injury claims. Significant associations were seen for male and middle-aged workers, workers in small and medium-sized enterprises, and those working in the manufacturing sector. And 1 °C increase in minimum temperature was associated with 1.7% (RR=1.017, 95%CIs 1.012-1.021) increase in daily injury claims. Significant associations were observed for female and middle-aged workers, workers in large-sized enterprises, and those working in the transport and construction sectors.

Conclusions: We found a higher risk of work-related injuries due to hot weather in Guangzhou, China. This study provides important epidemiological evidence for policy-makers and industry that may assist in the formulation of occupational safety and climate adaptation strategies.

Keywords: high temperature; work injury; case-crossover study; occupational health; climate change

Introduction

Climate change will pose significant health risks to workers in many ways, through increased heat exposure and non-heat related impacts, such as extreme weather events, shifts in disease vectors, industrial transitions and emerging industries [1-5]. The Intergovernmental Panel on Climate Change (IPCC) stated that there had been an overall increase in the number of warm days and nights at the global scale over the past decades [1, 6]. With a predicted increase in ambient temperature due to global warming, heat exposure is presenting a tremendous challenge for occupational health and safety in many countries [7-9].

Epidemiological studies have shown that workplace heat exposure can increase the risk of occupational injuries and accidents [4, 10, 11]. Occupational injury is a serious problem affecting the health of workers [12]. The International Labor Organization (ILO) estimates that worldwide 317 million workplace accidents occur each year, and the economic costs of work-related health problems including injuries are estimated to equal 4-6% of the gross domestic product (GDP) for most countries [13]. Recently, there have been growing concerns about the impact of heat stress on occupational health and safety under future climate change scenarios [14, 15].

Several previous studies have explored the associations between high temperature and work-related injury in Australia [16-19], Italy [20], Canada [21, 22] and the USA [23, 24]. Due to the availability of occupational health and safety data, all surveillance data based studies were from high-income countries. However, the relationship between temperature and work-related injury could vary by industries, gender and age groups in low- and middle-income countries, where socioeconomics, demographic characteristics and access to healthcare are much different from high-income countries. In particular, evidence shows that workers in low- and middle-income tropical countries are particularly vulnerable to climate change [25, 26].

The detailed analysis of occupational injury surveillance data can be a useful tool to investigate the effect of extreme weather on workers' health. In this study, we examined the association between high temperature and work injury using data from Guangzhou, a large subtropical city in China. We also aimed to identify which industrial sectors and sociodemographic groups are more vulnerable to hot weather.

Materials and Methods

Study settings

Guangzhou, with a resident population of 13.5 million and a labour force of 8.11 million in 2015, is the capital city of Guangdong Province. It is the main manufacturing hub of the Pearl River Delta in southern China, and also one of the leading manufacturing regions in the world. With a humid subtropical climate, Guangzhou is characterized by warm winters and hot summers, with plenty of rainfall and sunshine.

Data sources

Since the Regulations on Work Injury Insurance came into force on January 1, 2004, workers within the territory of the People's Republic of China participate in work-related injury insurance. As the scope of application of work injury insurance was limited, the State Council made significant changes to the Regulations on December 8, 2010 [27]. After that, the number of people who participate in work injury insurance scheme has been increasing steadily.

In this study, we obtained workers' injury claim data for Guangzhou from January 1, 2011, to December 31, 2012. The data included demographic and employment information (including age, gender and industry) and information on the occurrence of injuries (the company address at the district level and the date on which the injury occurred).

Weather data for Guangzhou including daily maximum and minimum temperatures, and daily average relative humidity were obtained from Guangzhou Bureau of Meteorology. In this study, we focused on two measures of temperature: daily maximum temperature and daily minimum temperature. Daily maximum temperature was used as a measure of heat exposure during the day of work. As daily minimum temperatures are typically reached around sunrise, it was used to measure the heat exposure during the sleep time before the day of work.

Data analysis

A time-stratified case-crossover design was used to estimate the association of heat exposure with work-related injury. The case-crossover study is a modification of the matched case-control study, where each person serves as his or her own control so that known and unknown time-invariant confounders, such as work experience, are inherently adjusted for by study design. In this study, temperature exposure for each case on the date of injury (case day) was compared to exposures when injury did not occur. Confining the control days to the month of injury reduces the influence of long-term time trends (e.g., industry power consumption). Control days were also limited to the same day of the week as for the case to adjust for day of the week. Consequently, there could be a maximum of 4 controls and a minimum of 3 controls before or after the case.

Due to our particular interest in heat effect, the study period was restricted to the warm seasons for Guangzhou (1 May-31 October). Using the time-stratified approach to referent day selection previously described, 731 case days were matched with a total of 2,488 referent days. In this way, each case day was matched with up to 4 referent days: 59.6% of cases were matched with 3 referent days, and 40.4% were matched with 4 referent days.

We used conditional Poisson regression models [28], which can allow for over-dispersion and autocorrelation, to analyze the association between temperature and injury risk. Daily maximum temperature and daily minimum temperature were put into separate regression models. Average humidity was included as a time-varying confounder in the models. Considering that previous studies reported non-linear heat-injury relationship, we initially assessed the relationship between temperature and injury risk for non-linearity by including a natural cubic spline with 3 df [29]. If the model did not indicate a non-linear relationship, we subsequently estimated the relationship between linear temperature increase and the risk of injury.

Additional analyses were performed on stratified data. We conducted separate models for each temperature metric by gender (male and female), age group (<25, 25-34, 35-44, 45-54 and ≥55) and occupational characteristics (business size). We also stratified our analyses by industrial sectors with mostly indoor or outdoor activities, as classified according to expert judgement.

Results for the conditional Poisson models are expressed as relative risks (RRs) with 95% confidence intervals (CIs), and interpreted as percentage change in daily injury claims per °C increase in temperature. Effects were considered statistically significant if the p-value <0.05. All analyses were conducted using R (version 3.4.0; R Foundation for Statistical Computing, Vienna, Austria).

Ethical Approval

This study was approved by the medical ethics committee of the School of Public Health, Sun Yat-sen University. Data used in the study were unidentifiable and individual patient consent was not required

Results

Overall, a total of 9,550 workers' compensation claims were identified in Guangzhou between 2011-2012, and 5,418 work-related injuries were included for analysis over the period of warm seasons. As shown in Table 1, the majority of claimants were male (77.2%) and aged 25-44 years (63.0%). About half (53.6%) of all injury claims occurred in the small enterprises. The percentage of injury claims for workers in manufacturing was 47%.

The daily average minimum and maximum temperatures during the study period were 24 °C and 32 °C, respectively. Figure 1 demonstrates the distribution of daily injury claims and outdoor temperatures for Guangzhou.

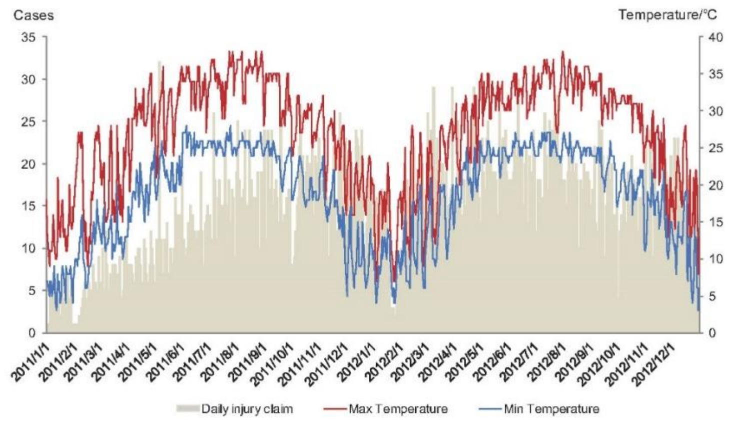


Figure 1. The distribution of daily injury claims and daily maximum and minimum temperatures in Guangzhou, China between 2011-2012. The grey column represents

daily injury claims. The red and blue line represents the daily maximum and minimum temperature, respectively.

Table 1. Numbers of workers' injury claims in Guangzhou, China between 2011–2012

Classification	Warm seasons	All seasons
Total	5418	9550
Gender		
Male	4207	7377
Female	1211	2173
Age group		
≤24	900	1541
25-34	1553	2753
35-44	1892	3327
45-54	932	1691
≥55	141	238
Business size[a]		
Small	2916	5119
Medium	1643	2908
Large	859	1523
Industrial sectors[b]		
Manufacturing	2555	4485
Finance, property and business services	1527	2683
Wholesale and retail trade	566	1021
Transport, storage and post	72	128
Construction	67	96
Others	631	1137

[a] The industry sector was categorized according to Classification of National Economic Sectors (GB/T 4754-2011).

[b] The business size was categorized according to Notice on Issuing the Provisions on the Classification Standard for Small and Medium-sized Enterprises (No. 300 [2011] of the Ministry of Industry and Information Technology, China).

Figure 2 shows the relative risks of work-related injury for temperature increase. A 1 °C increase in maximum temperature was associated with 1.4% (RR=1.014, 95%CIs 1.012-1.017) increase in daily injury claims. Increase of 1 °C in minimum temperature was associated with 1.7% (RR=1.017, 95%CIs 1.012-1.021) addition in daily injury claims.

Table 2 presents the associations between ambient temperature and work-related injury for all cases combined, demographic subgroups and occupational characteristic subgroups. Either maximum or minimum temperature was significantly associated with work-related injuries, but the associations varied in different subgroups. As shown in Figure 2, estimates presented are those of conditional Poisson regression models assuming linear temperature-injury relationships.

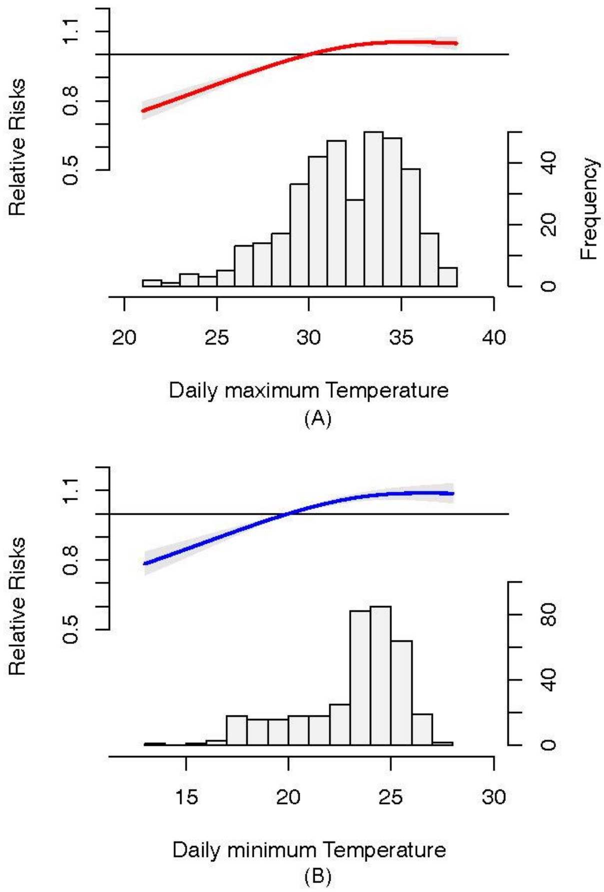


Figure 2. Associations[a] between daily maximum temperature and work-related injury risk (A), and minimum temperature and injury risk (B) with temperature distributions. The inserted histogram showed the frequency distribution of daily temperature. [a] Relative risk of injury for daily maximum temperature and minimum temperature, compared to the reference 30 °C and 20 °C, respectively, were estimated in the non-linear model with a natural cubic spline.

As in Table 2, for daily maximum temperature, daily claims increased by 1.4% for both male and female workers per °C increase. Among all age groups, workers aged 25-34, 35-44 and 45-54 were significantly associated with maximum temperature, by 1.8%, 2.1% and 0.9 % in injury claims per °C increase in maximum temperature. In contrast, no significant associations for workers aged <25 and ≥55 were observed.

Significant associations of daily maximum temperature with work injury were also observed in small and medium-sized enterprises, with daily claims increased by 1.4% and 1.7%, respectively, for each 1 °C increase in maximum temperature. In contrast, no significant association for large enterprises was found. Industry-specific analysis showed that there was a significant increase in injury claims with an increase in maximum temperature for 'manufacturing' (1.9%) and 'finance, property and business services' (1.4%).

For daily minimum temperature, associations of the temperature with work injury were also significant. Male and female workers, middle-aged workers (25-34 and 35-44 years), workers in large-sized enterprises were vulnerable to the minimum temperature. An interesting finding was significant associations among those working in outdoor industries such as 'transport, storage and post' and 'construction'.

Discussion

We found a positive relationship between high temperature and work-related injury in Guangzhou, China. Both maximum and minimum temperature were significantly associated with injury risk, but association sizes varied by worker group. To the best of our knowledge, this is the first study quantifying the impact of outdoor temperatures on work-related injuries in China.

In our study, per 1 °C increase in maximum temperature was associated with a 1.4% increase in daily injury claims. This finding is consistent with those reported by previous studies [18, 21]. Xiang et al [18] found a 1 °C increase in maximum temperature was associated with a 0.2% increase in daily injury claims in Adelaide, Australia, while Adam-Poupart et al. [21] modelled work-related injury compensations and outdoor temperature revealing a 0.2% increase with each increase of 1 °C in Quebec, Canada. The smaller association sizes in these studies could be explained by their temperate or cold climates.

Less clear is the mechanism by which maximum temperature exposure could be related to work injury. Physical and behavioural factors such as slippery, sweaty hands, foggy glasses, hot tools and working faster to avoid the heat may have acute impacts on injury risk [21, 30], but it could also be speculated that more sustained effects of heat are related to a combination of these physical issues with other factors such as fatigue and dizziness [30]. Future epidemiological research should continue to narrow the focus around cause-specific work injury to highlight potential important mechanisms.

We also found the significant positive associations between injury risk and daily minimum temperature. Such findings regarding the risk of occupational injury and minimum temperature are relatively new. The daily minimum temperature measures the minimum overnight temperature prior to the day of injury, which may reflect the influence of the sleeping thermal environment at night. There is accumulating evidence that sleep problems elevate the risk of injury in the workplace [31-33]. Sleep is essential for the body to recover from both physical and psychological fatigue suffered through the day and restore energy to maintain bodily functions. And thermal environment could be one of the most important factors that affect human sleep [34].

Maximum and minimum temperatures could be mutually confounded by daily weather. We examined this by a model in which maximum and minimum temperatures were co-adjusted. The estimates of minimum temperature did not change significantly if the maximum temperature was used as a confounding variable, but the results for maximum temperature do change. To avoid multicollinearity, however, we fitted maximum and minimum temperatures in separate regression models.

Table 2. Relative risks (RR) of work-related injury for per °C increase in daily temperature, Guangzhou, 2011-2012

	Daily Max. Temperature		Daily Min. Temperature	
	RR	95% CIs	RR	95% CIs
Total	**1.014**	1.012-1.017	**1.017**	1.012-1.021
Gender				
Male	**1.014**	1.011-1.016	**1.013**	1.009-1.018
Female	**1.015**	1.008-1.021	**1.030**	1.015-1.045
Age group				
<25	1.005	0.998-1.012	1.008	0.992-1.025
25-34	**1.018**	1.013-1.024	**1.027**	1.016-1.038
35-44	**1.021**	1.017-1.024	**1.012**	1.004-1.021
45-54	**1.009**	1.001-1.016	1.009	0.992-1.026
≥55	0.989	-	0.958	0.915-1.002
Business size				
Small	**1.014**	1.011-1.017	1.004	0.998-1.010
Medium	**1.017**	1.013-1.022	1.009	0.998-1.019
Large	1.003	0.995-1.011	**1.049**	1.029-1.068
Industrial sectors				
Sectors with mostly outdoor activities	.	.		
Transport, storage and post	1.008	0.987-1.029	**1.411**	1.335-1.493
Construction	1.001	0.979-1.024	**1.500**	1.426-1.580
Sectors with mostly indoor activities				
Manufacturing	**1.019**	1.015-1.022	1.002	0.994-1.010
Finance, property and business services	**1.014**	1.009-1.019	1.009	0.998-1.020
Wholesale and retail trade	1.008	0.996-1.020	1.094	1.065-1.125

*Bold represents significant p-values.

Our study suggests that both thermal comfort in workplaces, as well as the sleeping environment, may be important for occupational health. Although we could not find published data on this subject, it is possible that the effect of hot weather on occupational health and safety will be mediated through not only occupational heat stress at daytime but also sleeping thermal environment at night. In most regions, the frequency of warm days and nights will increase in the next decades [1]. Therefore, climate change is presenting and will continue to present occupational safety and health hazards to workers [35-37]. However, workers have received inadequate attention in the analysis of the impacts of climate change [9]. Additional surveillance, research and risk assessment are needed to characterize better and understand how occupational safety and health may be associated with climate events.

In our analyses, the vulnerable groups in workplaces during hot weather have been identified by gender, age group, business size and industry. The results indicate significant increases in injury claims for male workers with an increase in maximum temperature. Although previous studies have shown women to be less heat tolerant than men [38], male workers should also be a target in the preventive measurements for males being more likely to undertake high risky work. Age-specific analysis showed that the greater risk for the middle-aged workers (aged 35-44 years) might be because they are more intolerant to work-related heat than young individuals and often take more strenuous work than older people.

The analysis of business size showed that workers in small- and medium-sized enterprises were more vulnerable to work-related injuries with increasing maximum temperature, which is consistent with findings of previous research [18, 39]. In China, small- and medium-sized enterprises commonly lack effective cooling and ventilation system. In terms of industrial sectors, we showed that the sector with the greatest increased risk of work-related injury in association with temperature was manufacturing. These findings suggest that outdoor heat may add to the indoor temperature burden, which also results from heat-generating industrial processes, intense physical work and lack of cooling systems. Given our choice of the level of statistical significance, we could not find significant results for outdoor industrial sectors. This could be possibly due to the small number of injury claims for outdoor workers (less than 200). It was also possibly affected by high-temperature labour protection policies in Guangzhou (The People's Government of Guangdong Province, 2011) which advise the cessation of some outdoor work when the daily maximum temperature is above 39 °C.

In terms of labour protection, China is particularly interesting. To cope with intensive occupational heat exposure, China has released a new regulation: Administrative Measures on Heatstroke Prevention (AMHP2012) [40, 41]. The governmental regulation specifies the maximum temperature in the workplace and requires that employers pay high-temperature subsidies to workers in extremely hot environments. For example, according to the regulation in Guangzhou, employers are required to pay a subsidy to workers when the daily maximum temperature exceeds 35 °C. These measures could improve heat protection for workers, though research is still needed to evaluate the effectiveness of such policies (Zhao et al. 2016). The case in China is representative of many developing countries, which hold a dense population, experience severer and frequent heat exposure, and face rapid urbanization but have less capacity to adapt to climate change. Our study may arouse more attention on the health of people working under risky hot environments both indoors and outdoors.

There are several limitations to this study. The study uses temperature as an indicator of heat stress, without considering the influence of other factors that could play an important role. The most widely used heat stress index in occupational studies is the Wet Bulb Globe Temperature (WBGT) that considers air temperature, humidity, solar radiation and wind speed in a single index. The use of this index would have been preferable in our assessment as it would provide a more valid measure of total heat stress [42]. However, this index is not routinely measured, and we did not have the necessary data to estimate it. Secondly, we did not have information on the detailed conditions of the occurrence of injuries, such as the location (indoor or outdoor, the prevalence of air conditioning). This would have allowed for improved inferences on the potential impact of outdoor temperatures on indoor injuries. Thirdly, the Work Injury Insurance system is not universal, and the majority of migrant workers are not included in the system. Immigrants are widely distributed in the manufacturing, construction and other low-end labour markets, which may result in under-ascertainment of relevant injuries. Finally, the use of the case-crossover design, in which workers were matched to themselves, eliminated the potential for time-invariant confounding at the individual level, including confounding by socioeconomic status and time-invariant behaviour patterns, which is often a primary concern in work-related injury.

Conclusions

The risk of work-related injuries is significantly associated with hot weather in Guangzhou, China. In the context of climate change, increases in global temperatures and frequency of warm nights are expected, and the results of this study could be helpful to estimate future impacts of global warming on workers, as well as to develop climate adaptation strategies.

References

1. IPCC Climate Change 2014: Impacts, Adaptation, and Vulnerability; Cambridge University Press: Cambridge, UK and New York, NY, **2014**.
2. Schulte, P.; Bhattacharya, A.; Butler, C.; Chun, H. K.; Jacklitsch, B.; Jacobs, T.; Kiefer, M.; Lincoln, J.; Pendergrass, S.; Shire, J.; Watson, J.; Wagner, G. R., Advancing the Framework for Considering the Effects of Climate Change on Worker Safety and Health. *J Occup Environ Hyg* **2016**, 13, (11), 847-65.
3. Bennett, C. M.; McMichael, A. J., Non-heat related impacts of climate change on working populations. *Glob Health Action* **2010**, 3, 5640.
4. Kjellstrom, T.; Briggs, D.; Freyberg, C.; Lemke, B.; Otto, M.; Hyatt, O., Heat, Human Performance, and Occupational Health: A Key Issue for the Assessment of Global Climate Change Impacts. *Annu Rev Publ Health* **2016**, 37, 97-112.
5. UNDP Climate change and Labour: impacts of heat in the workplace; United Nations Development Program Geneva, **2016**.
6. Pal, J. S.; Eltahir, E. A., Future temperature in southwest Asia projected to exceed a threshold for human adaptability. *Nat Clim Change* **2016**, 6, (2), 197-200.
7. Kjellsreom, T.; Lemke, B.; Otto, M., Mapping Occupational Heat Exposure and Effects in South-East Asia: Ongoing Time Trends 1980–2011 and Future Estimates to 2050. *Ind Health* **2013**, 51, 56-67.
8. Hyatt, O. M.; Lemke, B.; Kjellstrom, T., Regional maps of occupational heat exposure: past, present, and potential future. *Glob Health Action* **2010**, 3.
9. Roelofs, C.; Wegman, D., Workers: the climate canaries. *Am J Ind Med* **2014**, 104, (10), 1799-801.
10. Xiang, J.; Bi, P.; Pisaniello, D.; Hansen, A., Health impacts of workplace heat exposure: an epidemiological review. *Ind Health* **2014**, 52, (2), 91-101.
11. Otte im Kampe, E.; Kovats, S.; Hajat, S., Impact of high ambient temperature on unintentional injuries in high-income countries: a narrative systematic literature review. BMJ Open 2016, 6, (2), e010399.
12. Wang, H.; Chen, G.; Wang, Z.; Zheng, X., Socioeconomic inequalities and occupational injury disability in China: a population-based survey. Int J Environ Res Public Health 2015, 12, (6), 6006-15.
13. WHO Protecting workers' health: Fact sheet N°389. http://www.who.int/mediacentre/factsheets/fs389/en/ (June 8),
14. Kjellstrom, T.; Freyberg, C.; Lemke, B.; Otto, M.; Briggs, D., Estimating population heat exposure and impacts on working people in conjunction with climate change. Int J Biometeorol 2017.
15. Watts, N.; Adger, W. N.; Ayeb-Karlsson, S.; Bai, Y.; Byass, P.; Campbell-Lendrum, D.; Colbourn, T.; Cox, P.; Davies, M.; Depledge, M.; Depoux, A.; Dominguez-Salas, P.; Drummond, P.; Ekins, P.; Flahault, A.; Grace, D.; Graham, H.; Haines, A.; Hamilton, I.; Johnson, A.; Kelman, I.; Kovats, S.; Liang, L.; Lott, M.; Lowe, R.; Luo, Y.; Mace, G.; Maslin, M.; Morrissey, K.; Murray, K.; Neville, T.; Nilsson, M.; Oreszczyn, T.; Parthemore, C.; Pencheon, D.; Robinson, E.; Schütte, S.; Shumake-Guillemot, J.; Vineis, P.; Wilkinson, P.; Wheeler, N.; Xu, B.; Yang, J.; Yin, Y.; Yu, C.; Gong, P.; Montgomery, H.; Costello, A., The Lancet Countdown: tracking progress on health and climate change. Lancet 2017, 389, (10074), 1151-1164.
16. McInnes, J. A.; MacFarlane, E. M.; Sim, M. R.; Smith, P., The impact of sustained hot weather on risk of acute work-related injury in Melbourne, Australia. Int J Biometeorol 2017.

17. McInnes, J.; Akram, M.; MacFarlane, E.; Keegel, T.; Sim, M. R.; Smith, P., Association between high ambient temperature and acute work-related injury: a case-crossover analysis using workers' compensation claims data. Scand J Work Env Hea 2016, 43, (1), 86-94.
18. Xiang, J.; Bi, P.; Pisaniello, D.; Hansen, A.; Sullivan, T., Association between high temperature and work-related injuries in Adelaide, South Australia, 2001-2010. Occup Environ Med 2014, 71, (4), 246-52.
19. Xiang, J.; Bi, P.; Pisaniello, D.; Hansen, A., The impact of heatwaves on workers' health and safety in Adelaide, South Australia. Environ Res 2014, 90-95.
20. Marco, M.; Lorenzo, C.; Alfonso, C.; Pietro, A. M.; Simone, O., Relationship between Work-Related Accidents and Hot Weather Conditions in Tuscany (Central Italy). Ind Health 2006, 44, 458-464.
21. Adam-Poupart, A.; Smargiassi, A.; Busque, M.; Duguay, P.; Fournier, M.; Zayed, J.; Labreche, F., Effect of summer outdoor temperatures on work-related injuries in Quebec (Canada). Occup Environ Med 2015, 72, (5), 338-45.
22. Fortune, M.; Mustard, C.; Brown, P., The use of Bayesian inference to inform the surveillance of temperature-related occupational morbidity in Ontario, Canada, 2004–2010. Environ Res 2014, 449-456.
23. Spector, J.; Bonauto, D.; Sheppard, L.; Busch-Isaksen, T.; Calkins, M.; Adams, D.; Lieblich, M.; Fenske, R. A., A Case-Crossover Study of Heat Exposure and Injury Risk in Outdoor Agricultural Workers. PLoS One 2016, 11, (10), e0164498.
24. Garzon-Villalba, X.; Mbah, A.; Wu, Y.; Hiles, M.; Moore, H.; Schwartz, S. W.; Bernard, T. E., Exertional heat illness and acute injury related to ambient wet bulb globe temperature. Am J Ind Med 2016, 59, (12), 1169-1176.
25. Kjellstrom, T.; Holmer, I.; Lemke, B., Workplace heat stress, health and productivity - an increasing challenge for low and middle-income countries during climate change. Glob Health Action 2009, 2.
26. Kjellstrom, T., Climate change, direct heat exposure, health and well-being in low and middle-income countries. Glob Health Action 2009, 2.
27. ILO National Profile Report on Occupational Safety and Health in China; International Labour Organization: Geneva, 2012.
28. Armstrong, B. G.; Gasparrini, A.; Tobias, A., Conditional Poisson models: a flexible alternative to conditional logistic case cross-over analysis. BMC Med Res Methodol 2014, 14, (122).
29. Barnett, A. G.; Stephen, D.; Huang, C.; Wolkewitz, M., Time series models of environmental exposures: Good predictions or good understanding. Environ Res 2017, 154, 222-225.
30. Pilcher, J. J.; Nadler, E.; Busch, C., Effects of hot and cold temperature exposure on performance: a meta-analytic review. Ergonomics 2002, 45, (10), 682-98.
31. Uehli, K.; Mehta, A. J.; Miedinger, D.; Hug, K.; Schindler, C.; Holsboer-Trachsler, E.; Leuppi, J. D.; Kunzli, N., Sleep problems and work injuries: a systematic review and meta-analysis. Sleep Med Rev 2014, 18, (1), 61-73.
32. Uehli, K.; Miedinger, D.; Bingisser, R.; Durr, S.; Holsboer-Trachsler, E.; Maier, S.; Mehta, A.; Muller, R.; Schindler, C.; Zogg, S.; Kunzli, N.; Leuppi, J., Sleep problems and work injury types: a study of 180 patients in a Swiss emergency department. Swiss med wkly 2013, 143, w13902.
33. Salminen, S.; Oksanen, T.; Vahtera, J.; Sallinen, M.; Harma, M.; Salo, P.; Virtanen, M.; Kivimaki, M., Sleep disturbances as a predictor of occupational injuries among public sector workers. J Sleep Res 2010, 19, (1 Pt 2), 207-13.
34. Lan, L.; Pan, L.; Lian, Z.; Huang, H.; Lin, Y., Experimental study on thermal comfort of sleeping people at different air temperatures. Build Environ 2014, 73, 24-31.

35. Luo, H.; Turner, L. R.; Hurst, C.; Mai, H.; Zhang, Y.; Tong, S., Exposure to ambient heat and urolithiasis among outdoor workers in Guangzhou, China. Sci Total Environ 2014, 472, 1130-6.
36. Sett, M.; Sahu, S., Effects of occupational heat exposure on female brick workers in West Bengal, India. Glob Health Action 2014, 7, 21923.
37. Sahu, S.; Sett, M.; Kjellstrom, T., Heat Exposure, Cardiovascular Stress and Work Productivity in Rice Harvesters in India: Implications for a Climate Change Future. Ind Health 2013, 51, (4), 424-431.
38. Mathee, A.; Oba, J.; Rose, A., Climate change impacts on working people (the HOTHAPS initiative): findings of the South African pilot study. Glob Health Action 2010, 3.
39. Lundgren, K.; Kuklane, K.; Gao, C.; Holmer, I., Effects of heat stress on working populations when facing climate change. Ind Health 2013, 51, (1), 3-15.
40. The State Administration of Work Safety; et al. The Administrative Measures on Heatstroke Prevention. www.chinasafety.gov.cn/newpage/Contents/Channel_5912/2012/0704/172994/content_172994.htm (May 24),
41. Zhao, Y.; Sultan, B.; Vautard, R.; Braconnot, P.; Wang, H. J.; Ducharne, A., Potential escalation of heat-related working costs with climate and socioeconomic changes in China. P Natl Acad Sci USA 2016, 113, (17), 4640-5.
42. Gao, C.; Kuklane, K.; Ostergren, P. O.; Kjellstrom, T., Occupational heat stress assessment and protective strategies in the context of climate change. Int J Biometeorol 2017.

2.2 Estimation of work-related injury and economic burden attributable to heat stress in Guangzhou, China

Rui Ma [1,#], Shuang Zhong [2,#], Marco Morabito [3,4], Shakoor Hajat [5], Zhiwei Xu [1], Yiling He [1], Junzhe Bao [1], Rongrong Sheng [1], Changchang Li [1], Chuandong Fu [6,*], Cunrui Huang [1,*]

[1] School of Public Health, Sun Yat-sen University, Guangzhou, China;
[2] Center for Chinese Public Administration Research, School of Government, Sun Yat-sen University, Guangzhou, China;
[3] Institute of Biometeorology, National Research Council, Florence, Italy;
[4] Centre of Bioclimatology, University of Florence, Florence, Italy;
[5] Department of Public Health, Environments and Society, London School of Hygiene & Tropical Medicine, London, UK;
[6] Guangdong Provincial Work Injury Rehabilitation Hospital, Guangzhou, China.
[#] These authors contributed equally to this work.
[*] Correspondence: huangcr@mail.sysu.edu.cn (C. Huang), fucd168168@163.com (C. Fu).

Ma R, Zhong S, Morabito M, Hajat S, Xu Z, He Y, et al. Estimation of work-related injury and economic burden attributable to heat stress in Guangzhou, China. Science of The Total Environment 2019;666:147-154.

Abstract:

Background: Climate change has exacerbated the health effects of high ambient temperatures on occupational health and safety; however, to what extent heat stress can induce workplace injuries and economic costs is poorly studied. This study aimed to quantify the attributable fractions of injury claims and subsequent insurance payouts using data from work-related injury insurance system in Guangzhou, China.

Methods: Individual workers' injury claims data were collected from 2011 to 2012, including demographic characteristics and work-related information. Daily maximum wet bulb globe temperature (WBGT, °C) were calculated from meteorological data. To examine the association between WBGT index and work-related injury, we fit a quasi-Poisson regression with distributed lag non-linear model. Then we calculated the numbers of injury claims and costs of insurance compensations attributable to days with WBGT above the heat stress limit according to the national occupational health standards.

Results: There were 9,550 work-related injury claims, resulting in an insurance payout of 282.3 million Chinese Yuan. The risks of injury claims increased with rising WBGT. 4.8% (95% eCI: 2.9% - 6.9%) of work-related injuries and 4.1% (95% eCI: 0.2% – 7.7%) of work-related injury insurance payouts were attributed to heat exposure for WBGT threshold above the heat stress limit. Male workers, those in small enterprises and with low educational attainment were especially sensitive to the effects of heat exposure.

Conclusions: Heat stress can contribute to a higher risk of work-related injury and substantial economic costs. Quantified the impacts of injuries and related economic costs should be considered to develop targeted preventive measures in the context of climate change.

Keywords: climate change; heat stress; occupational health; work-related injury; economic cost

Introduction

As our climate continues to warm [1], heat-related health burdens are expected to rise. A large number of epidemiological studies demonstrated that high temperatures increase both mortality and morbidity [2-6], and these relationships are often applied to climate projection data to estimate future health burdens [7]. However, a big unknown is the degree to which current relationships will still hold once ambient temperatures begin to surpass levels that general populations are currently exposed to and limits to adaptability are potentially reached [8]. Studies from occupational health settings can offer insight into such patterns since exposures to heat are often far higher [9].

As physiology-based studies show, dissipation of internal heat generation during strenuous activity is vital to human health [10, 11], and heat exposure from the ambient environment can exacerbate heat stress amongst those constantly exposed such as outdoor workers [12]. With the accumulation of heat stress, core body temperature can exceed the safe and acceptable thermal limits of 37 °C, not only leading to acute health issues, such as heat exhaustion and heat stroke but also increased risks of work-related injury and occupational diseases [13-15]. Impaired workers' health may also lead to limited working capacity, resulting in productivity and economic loss. It is estimated that heat-related work absenteeism and performance reduction can result in an economic loss equivalent to 6.2 billion US Dollars (USD) for the Australian workforce, which is about from 0.33 to 0.47% of its GDP [16]. Xia et al. [17] also found that the severe heat waves of 2013 in Nanjing caused a total of 27.5 billion Chinese Yuan (CNY) of economic losses, equating to 3.4% of the city's gross value of production.

Previous studies have observed significant effects of heat exposure on work-related injuries in Adelaide, Australia [18], Tuscany, Italy [19], and Quebec, Canada [20]. Sheng et al. [12] found that both hot days and warm nights increased work-related injury risks in China. Additionally, Matinez-Solanas et al. [21] quantified non-optimal ambient temperature related injuries and associated economic burden in Spain, showing that heat posed more danger than cold in occupational settings. Xiang et al. [22] found a significant increase in medical costs and work-days lost due to occupational heat-induced illness. Although the health impacts of ambient heat exposure on work-related injury are of growing interest, there is little research focusing on the economic loss of high temperatures because of injury [21, 22]. Furthermore, where losses are quantified, these are mainly based on estimated economic costs and burdens rather than actual costs [21], thus introducing considerable uncertainty.

As the Earth's climate continues to change and workers will be exposed to ever-increasing ambient temperatures, it is crucial to evaluate variations in heat-related health impacts and economic losses in occupational health settings; so that governments can develop targeted labour protection policies to protect the health and reduce the productivity loss. In this study, we aim to quantify the impact of heat stress on work-related injury claims, also assessing subsequent economic costs in one of the most populous cities in southern China.

Materials and Methods

Study setting

Guangzhou is one of ‘the biggest cities in China, and one of the major manufacturing centres in the world. With a population of more than 14 million and a labour force of 8.35 million in 2016, the GDP of Guangzhou reached 2,150 billion CNY in 2017 (330 billion USD), ranking fourth in all Chinese cities. Located in a sub-tropical monsoon climate region, Guangzhou usually experiences long summer with high temperatures and abundant rainfall. The monthly average temperatures are above 28 °C (the monthly average maximum temperature is even higher than 33 °C) during July and August. In these months, the monthly mean values of relative humidity are close to 80%. This situation often contributes to creating average thermal conditions during summer months characterized by moderate and strong heat stress.

Work-related Injuries Data

In this study, we used a retrospective study design. We obtained de-identified worker injury claim data of Guangzhou from the work-related injury insurance system, referred to the period January 1, 2011 to December 31, 2012. This data includes demographic characteristics (age, gender, and educational attainment) and work-related information (enterprise name, size and industry type), the date of injury occurrence, the assessment of injury severity and the total amount of insurance payouts. The daily insurance payouts were then calculated by aggregating amounts of individual payouts and also showed as USD with the exchange rate of December 31, 2012 (1 CNY = 0.16 USD). Educational attainment was categorized into three levels: low education (middle school and below, which is a compulsory education); intermediate education (high school or higher vocational college), and high education (university or postgraduate education). Injured workers were diagnosed for their gradation of disability with the national standard “Standard for identify work-ability – Gradation of disability caused by work-related injuries and occupational diseases” (GB/T 16180-2006) issued by Ministry of Labor and Social Security, China [23] and were classified into eleven degrees. It is then categorized into three groups of injury severity according to the functionality of each degree: 1) the minor injury group, including people who did not take the impairment identification or those whose disability did not reach the mildest class; 2) the medium injured group, including people who were classified as degree 10 (the mildest class of disability, their physical function did not lead to permanent damage); and 3) the severely injured group, including people whose identification conclusion were degree 9 to degree 1 (the most serious degree of disability, they suffered from the injury and had permanent dysfunction).

Weather Data

Daily maximum wet bulb globe temperature (WBGT) values were obtained for the city of Guangzhou by using the Hothaps-Soft (High occupational temperature health and productivity suppression) database and software, provided by ClimateSoft Ltd [24]. This software obtains meteorological data from NOAA/GSOD (US National Oceanographic and Atmospheric Administration/Global Surface Summary of the Day) and calculates the indoors or full shade WBGT index with the method introduced by Bernard et al. [25].

The WBGT (unit = °C) is a well-established heat stress index that considers the combination of several important microclimate variables useful for heat-stress assessment, such as the natural wet-bulb temperature (Tnwb, °C, that represents the largest component of WBGT), the black globe temperature (Tg, °C) and the dry-bulb temperature (Ta, °C). Today, the WBGT represents the most commonly used heat stress index for workplace applications [26-28] and is also used in international standards [ISO, 29].

Despite its wide usage in international heat stress standards and occupational research, WBGT index is still not a meteorological indicator routinely measured. However, several calculation methods using regular meteorological data have been published [25, 30, 31].

Statistical Analysis

All individual claims were transformed into daily time-series data and grouped by their demographic characteristics, and then merged with meteorological data. A quasi-Poisson regression allowing for over-dispersion with a distributed lag non-linear model (DLNM) [32] was applied to examine the association between heat stress (WBGT values) and work-related injuries. This approach allows for considering the over-dispersed Poisson distribution of injuries, also accounting for the non-linear association, typical in this kind of investigations, and the potential delayed effect of heat stress. The same approach was used to model the association between heat exposure (WBGT values) and insurance payouts.

The analyses were conducted using the DLNM package (2.3.2) [33] in R 3.4.0 [34].

The median value of daily maximum WBGT during the whole study period (24 °C) was used as the reference threshold (centring value) for fitting the exposure-response relationship. Then relative risks at 30°C were reported. We modelled the exposure-response curve with a natural cubic spline with two internal knots placed at equal spaces. The maximum WBGT index was included in the model as cross-basis function. A natural cubic spline of time was used to control for time trend and seasonality and a dummy variable for the year was used to adjust for inter-year trends. Other dummy variables for day of the week and public holidays were also fitted in the model.

According to the occupational health standard Occupational exposure limits for hazardous agents in the workplace (GBZ 2.2-2007) issued by Ministry of Health of China [35], 8 hours' full-time work can be conducted safely even for very high work activities when the WBGT at the workplace does not exceed 25 °C. For jobs requiring high, moderate and light physical workload, WBGT thresholds of 26 °C, 28 °C and 30 °C, were selected respectively according to the standard. Detailed information was presented in Table S1 and Table S2 of supplemental material.

As the heat-related health effect is generally immediate or occurs on a very short time scale, a time lag of zero-day was used in the primary analyses. However, models were also fit by setting maximum time lag periods of 3 and 7 days in the sensitivity analyses to assess possible delayed effects. Other models with different knots and degrees of freedom were also considered in our sensitivity analyses.

To calculate the measures of injury claims and the cost of compensation attributable to high WBGT values, the daily maximum WBGT and the corresponding relative risks were combined to assess the attributable numbers of each day. Finally, the attributable number over the heat stress limit of 25 °C was summed, and 95% empirical confidence intervals (eCI) were provided [36].

Results

Table 1 shows the descriptive statistics for the workers' compensation claims in Guangzhou between 2011 and 2012. In total, 9,550 claims occurred during the study period, resulting in an insurance payout of 282.3 million CNY, which equates to 29.6 thousand CNY per injury. About 47%, 28% and 25% of all injuries were classified into the minor, medium and severe injury, respectively. The average insurance payout for severe injuries (72.5 thousand CNY) was higher than for medium injuries (29.4 thousand CNY) and minor injuries 7.1 thousand CNY). There were 4,008 injury claims in 2011 and 5,542 in 2012, which resulted in an average payout of 33.3 and 26.8 thousand CNY, respectively.

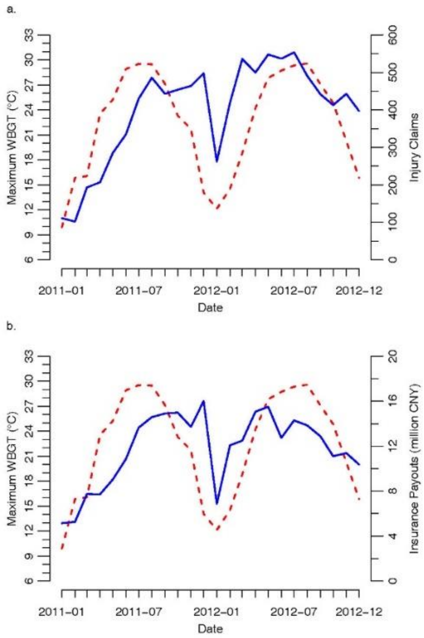


Figure 1. The time-series of monthly median of maximum WBGT (red dashed line, in both Panel a & b), work-related injury claims (solid blue line, in Panel a), and

insurance payouts (blue solid line, in Panel b) during 2011-2012, in Guangzhou, China.

Table 1. Numbers of works' injury claims and insurance payouts during 2011-2012 in Guangzhou, China.

Variables	Injury Claims (%)	Insurance Payouts (million CNY)
Total	9,550 (100)	282.3
Gender		
Male	7,377 (77.2)	228.6
Female	2,173 (22.8)	53.6
Age group		
<35	4,294 (45.0)	116.3
35-44	3,327 (34.8)	101
>44	1,929 (20.2)	65
Educational attainment		
Low	5,378 (56.3)	157.5
Intermediate	3,033 (31.8)	91.4
High	1,139 (11.9)	33.4
Business size		
Small	5,119 (53.6)	158.4
Middle	2,908 (30.5)	85.8
Large	1,523 (15.9)	38
Injury severity		
Minor	4,524 (47.4)	32
Medium	2,648 (27.7)	78
Severe	2,378 (24.9)	172.4

Note: CNY, Chinese Yuan. 1 Chinese Yuan = 0.16 US Dollar (Exchange rate of December 31, 2012). The business size was categorized according to the Provisions on the Classification Standard for Small and Medium-sized Enterprises (No. 300 [2011]) of the Ministry of Industry and Information Technology, China).

Daily maximum WBGT index ranged from 5.7 °C to 31.3 °C, with a mean value of 22.4 °C and a median value of 24 °C during the 2 years (Fig. 1). Monthly averaged maximum WBGT was higher than 24°C during the warm season (May 1 – October 31). There were more than 46% of days (339 days) during which the daily maximum WBGT index exceeded 25 °C (the threshold for reducing working hours during very high labour activities), and 7.5% of days (55 days) during which the maximum WBGT index exceeded 30 °C, that is the threshold for reducing working hours of light workload.

Relative risks (RR) of overall injury claims increased with successive increases in WBGT values, reaching 1.15 at the threshold of 30 °C (95% CI: 1.08 - 1.22) (Fig. 2). It is estimated that 4.8% of work-related injury claims are attributable to heat exposure above the WBGT threshold of 25°C (Table 2), corresponding to 461 injuries (95% eCI: 257 - 658) in the study period. About 11.6 million CNY (95% eCI: 0.6 - 21.2) used for insurance payouts could be attributed to WBGT values above 25°C, which represents approximately 4.1% of the total work-related injury insurance payouts during the study period.

High relative risks of work-related injuries and insurance payouts increasing with the WBGT were observed (Fig. 3 and 4). Male (RR: 1.15, 95% CI: 1.1 - 1.23) and female (RR: 1.14, 95% CI: 1.01 - 1.29) workers had similar risks of injury with increased the WBGT (Fig. 3), while female only accounted for 22.8% of total injury claims. Among all age groups, workers aged 35 to 44 were most sensitive to the increase of heat stress (RR: 1.16, 95% CI: 1.06 - 1.28), followed by workers under 35 years old (RR: 1.14, 95% CI: 1.04 - 1.24) (Fig. 3). On the other hand, the relationship between work-related injuries in workers older than 44 years old was not statistically significant (RR: 1.15, 95% CI: 0.99, 1.32). Workers with intermediate educational attainment showed the highest work-related injury risks with increasing WBGT (RR: 1.19, 95% CI: 1.08 - 1.32), followed by workers with low educational attainment (RR: 1.14, 95% CI: 1.05 - 1.23). Though elevated with increasing WBGT, the injury risk of workers with high educational attainment was statistically significant only at a WBGT value of 25 °C (RR: 1.02, 95% CI: 1.00 - 1.04).

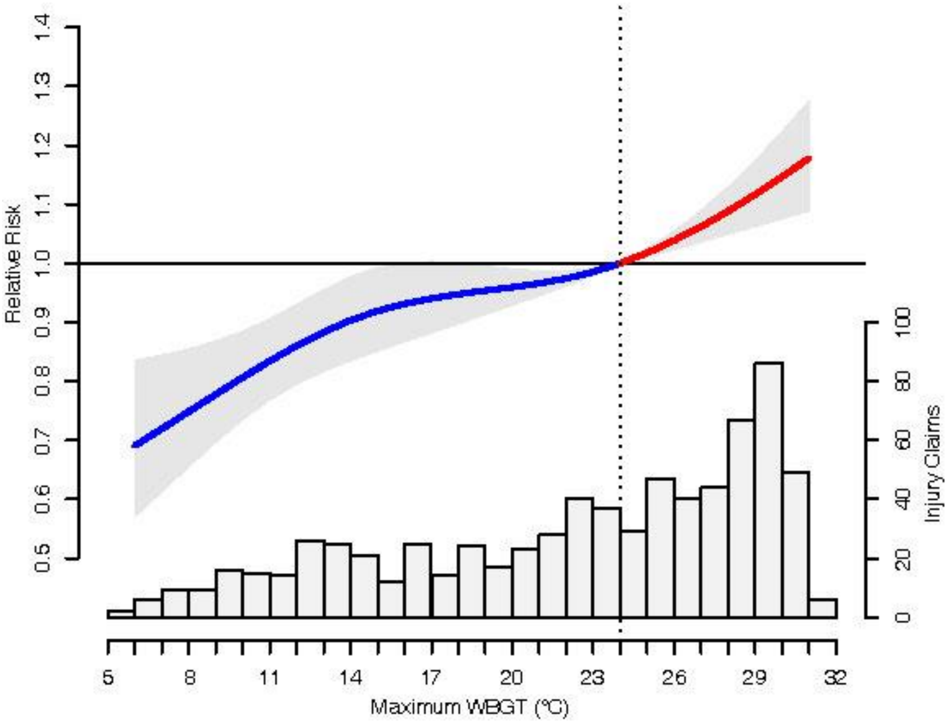


Figure 2. The exposure-response relationship between daily maximum WBGT index and injury claims.

As for business size, workers in small enterprises were most sensitive to the effect of high WBGT thresholds (RR: 1.17, 95% CI: 1.08 - 1.27), followed by workers employed in medium-sized enterprises (RR: 1.16, 95% CI: 1.04 - 1.29). No significant associations were found for workers engaged in large enterprises (RR: 1.06, 95% CI: 0.91 - 1.23) (Fig. 3).

Table 2. Work-related injuries and insurance payouts attributable to heat stress above the WBGT limit (25 °C).

Classification	**Attributable Fraction** (95% eCI)	**Attributable Number** (95% eCI)
Total	4.8 (2.9 - 6.9)	461 (257 - 658)
Gender		
Male	4.9 (2.8 - 7.1)	364 (208 - 522)
Female	4.5 (0.8 - 8.1)	98 (15 - 182)
Age group		
<35	4.7 (1.7 - 7.6)	201 (68 - 318)
35-44	5.2 (2.0 - 8.2)	174 (72 - 272)
>44	4.5 (-0.3 - 8.6)	87 (-3 - 161)
Educational attainment		
Low	4.3 (1.6 - 6.7)	231 (92 - 367)
Intermediate	6.2 (3.0 - 9.3)	189 (95 - 285)
High	3.6 (-2.2 - 8.9)	41 (-30 - 97)
Business size		
Small	5.5 (2.9 - 8.01)	280 (145 - 401)
Middle	5.2 (1.6 - 8.4)	152 (49 - 243)
Large	2.0 (-3.6 - 6.6)	30 (-60 - 100)
Injury severity		
Minor	7.7 (5.0 - 10.2)	348 (220 - 464)
Medium	1.2 (-2.7 - 4.7)	33 (-68 - 119)
Severe	4.0 (-0.2 - 7.8)	96 (0 - 184)
Insurance payout (million CNY)	4.1 (0.2 - 7.7)	11.58 (0.6 - 21.2)

Note: 95% eCI, 95% empirical confidence intervals; CNY, Chinese Yuan. 1 Chinese Yuan = 0.16 US Dollar (Exchange rate of December 31, 2012). The business size was categorized according to the Provisions on the Classification Standard for Small and Medium-sized Enterprises (No. 300 [2011]) of the Ministry of Industry and Information Technology, China).

The investigation of different injury severities showed higher risks in the minor injured group (RR: 1.24, 95% CI: 1.14 - 1.35) (Fig. 3). Significantly increased risks were also observed in severely injured workers, except for the value at the threshold of 30 °C (RR: 1.12, 95% CI: 0.99 - 1.28).

Similar trends were also observed considering the relationships between increasing heat stress and insurance payouts, though few results were statistically significant, such as female workers (RR: 1.33, 95% CI: 1.05 - 1.68), workers employed in medium-sized enterprises (RR: 1.3, 95% CI: 1.07 - 1.58), and workers with intermediate educational attainment (RR: 1.33, 95% CI: 1.09 - 1.64). Adverse trends were observed in workers with high educational attainment. With increased WBGT index, their relative risk decreased (RR: 0.79, 95% CI: 0.59 - 1.07), although not statistically significantly (Fig. 4).

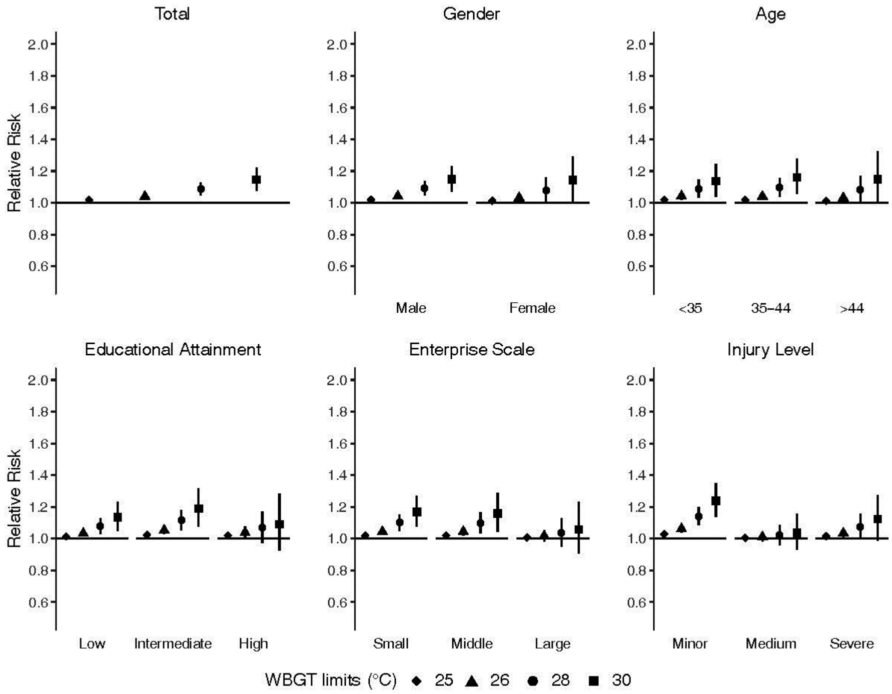


Figure 3. Relative risks of work-related injuries at different heat stress limits. (Compared to the reference WBGT at 24 °C)

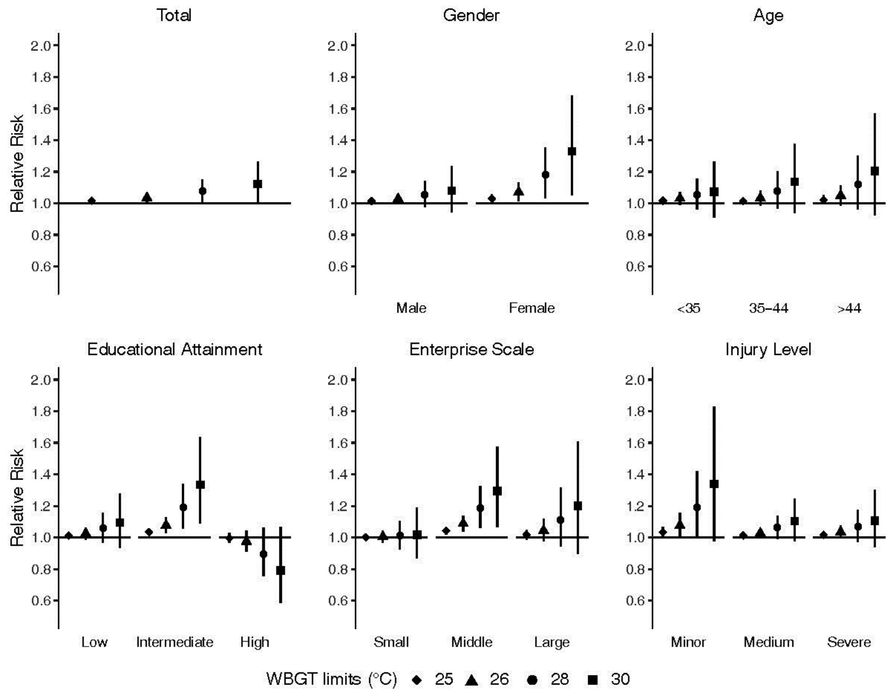


Figure 4. Relative risks of insurance payouts at different heat stress limits. (Compared to the reference WBGT at 24 °C)

Models with different lag periods, knots and degrees of freedom were also used as sensitivity analyses in Table S3. The results were robust according to sensitivity analyses.

Discussion

This is the first Chinese study quantifying work-related injuries and associated economic costs attributable to workplace heat exposure. Our findings showed that high WBGT values were associated with increased incidence of health impairments in occupational population, resulting in excessed work-related injuries and insurance payouts in Guangzhou, China.

These results partially confirm previous studies [12, 18-20, 37, 38] which found increased injury risks with rising temperatures. However, only a few studies have quantified the fraction of work injury attributable to heat stress, and to the best of our knowledge, no study assessed the actual economic costs associated with heat-related work injuries. Xiang et al. [22] investigated illness directly induced by heat and found this illness only accounted for 0.1% of all injury claim, and 0.04% of total compensation costs. Martínez-Solanas et al. [21] were the first to calculate occupation injuries attributable to ambient temperature in Spain and found that 2.4% of occupational injuries were attributed to moderate and extreme heat conditions. In the present study, the fraction of work-related injury claims attributed to heat exposure was 4.8%, twice compared to the average value observed in Spain, but similar to results of some southern Spain provinces, those provinces have mild winters and hot summers, which is similar to the climate conditions of Guangzhou. Falling into the subtropical monsoon climate belt, Guangzhou has hot and very humid (also rainy) summer. In particular, the monthly average maximum WBGT from May to October is above 24 °C. These heat stress conditions pose adverse health effects on workers, especially for those exposed to the outdoor environment.

As for economic costs, our analysis showed that 4.1% of injury insurance compensation cost was attributed to heat stress. However, our data only contained insurance payouts; the medical fees and subsidies are only a small portion of high ambient temperature-related economic burden [21]. Thus the economic burden of work-related injury in this research was underestimated, and potential costs of mental distress and productivity loss need to be taken into consideration [39].

In this study, we used the WBGT index to estimate the heat exposure of workers. The heat transfer processes of human include evaporation, convection and radiation, and these phenomena are influenced by temperature differences, humidity and wind speed. Previous studies generally used the ambient air temperature with humidity controlled [18, 20, 37], but the use of WBGT allows a more in-depth thermal stress analysis through the consideration of the air humidity and wind speed (and also solar radiation if available), in this way providing a complete picture of heat stress. Another advantage of using WBGT index is that it provides comparability between results and it represents an official occupational health Chinese standard "Occupational exposure limits for hazardous agents in the workplace" (GBZ 2.2-2007). Our results showed that in 46% of days, during the study period, the daily maximum WBGT index exceeded the recommended WBGT threshold that requires a reduction of working hours for the high workload that often involves farmers and construction workers for which preventive and protective measures are necessary.

According to the subgroup analysis, male workers underwent slightly higher injury risk than female workers, while claim costs of female workers were more influenced by high heat stress conditions. However, considering the large number of male workers, it is of great importance to take targeted measures to protect male workers against workplace heat stress. The higher heat-related risk of male was similar to previous studies [18, 20, 37], which can be explained by differences in the type and intensity of work between the genders. Men are more likely to do physically demanding jobs, and undertake jobs in harsh environment, which makes them at higher risk in hot weather. Meanwhile, physical structure differences lead to more serious consequences among injured women, as well as greater insurance payouts. Previous studies found female workers were more likely to suffer from heat stress exposure at work [40], with higher claim costs [41].

The highest risk of heat-related work injury observed in workers with less than 45 years is also confirmed by recent studies [18, 21, 37]. Young workers are usually involved in more prolonged outdoor activities, exposing them at higher injury risk [42, 43]. However, the analyses which showed the increasing trends of insurance payouts were not statistically significant, suggesting larger sample size were needed to investigate the effects of high heat stress.

In addition, we only observed that workers with intermediate- or low-level educational attainment were vulnerable to heat exposure. One plausible explanation is that workers with high educational attainment are more likely to work at well-equipped workplaces with air-conditioning, while workers with low educational attainment are more likely to participate in manual works, exposing them more to high heat exposure conditions and undertaking more internal heat generated by labour processes. High educational attainment may also allow workers to have a better awareness of health protection to take care of themselves, taking more breaks and hydrating themselves better during hottest days.

Our analysis on business size indicates that workers in large enterprises seemed less likely to be affected by hot days compared with workers in small or middle enterprises, which is consistent with Xiang et al. [18]. In general, large companies usually have improved facilities, regular safety education training and strict enforcement of labour protection. Meanwhile, the only significant elevation of insurance payout was observed in middle-size enterprises, and this may be related to the complete injury report system compared to small enterprises. Therefore, more attention should be paid to small- and middle-size enterprises during hot work conditions.

Results related to the injury severity suggest the highest risk for minor injuries. Minor injury usually follows neglecting and mistake, such as hitting objects or being hit by moving objects [44, 45]. These results suggest that more importance should be given to minor injuries mainly because of their increased frequency and preventability.

We found no evidence of delay effect between high WBGT index and injury claims. This is consistent with results of Xiang et al. [18] but different from the study of Adam-Poupart et al. [20] which reported that heat effect on work injuries occurred two-three days after exposure. Unlike the general population, workers usually have higher metabolic rate during labour works, undertake direct and immediate impacts from ambient heat [8], and their adaptive responses to the heat stress are restricted due to work duties [46]. Thus the acute effect is dominant in occupational heat-related injury.

Some mechanism about heat stress-induced injuries has been explained [8]. During hot days, the increasing body sweat represents a cooling method, which might cause dehydration, result in distraction, slow reaction, dizziness etc. [47]. Sweaty tools and devices are harder to operate, which may lead to accidents too [15]. Additionally, personal protective equipment (PPE) often hinders heat dissipation and increases heat strain [48]. Small companies are unlikely to have complete equipment and regulations, while people at younger ages or with low educational attainment might lack experience, which can make them more vulnerable to heat stress. Other factors may also play important roles in the incidence of work-related injuries, such as poor health status [49, 50], lacking work experience [51, 52], physical exertion [43], absence of training course [53] and personal protective equipment [54, 55], and these factors may modify the association between heat stress and work-related injury.

Over the past decade, the Chinese government has increasingly recognized heat stress as a factor of an occupational hazard, and preventive measures have been taken to protect the workers' health and productivity. In the occupational health Chinese standard GBZ 2.2-2007 [35], jobs are divided into 4 work types based on their physical workload and recommended work-rest schedules are provided depending on different WBGT thresholds. For example, the duration of very high workload is reduced to 6 hours when the workplace WBGT reaches 26 °C. The standard of GBZ 2.2-2007 was set based on the heat stress conditions in the workplace. However, few enterprises conduct these monitoring work routinely, thus reducing the effectiveness of prevention in practice.

Increased environmental heat levels have posed a severe impact on human health and global economy, and future climate change scenarios reveal that workers engaged in various parts of the world will face significant increasing of thermal stress levels. The work capacity of in-shade workers with moderate physical workload can decrease 2.04% under RCP 6.0 scenario during 2071-2099 [56], and effective measures to protect workers from injuries in the context of global warming were needed to reduce the adverse health impacts related to the increasing temperature [27].

Some limitations of this study should be acknowledged. Firstly, the WBGT index was calculated from meteorological data [25] rather than measured at the workplace. With appropriate models, however, WBGT derived from standard meteorological data can express the heat stress of the workplace better than single temperature indicator [30]. Secondly, limited coverage of work-related injury insurance is noteworthy; only 54% of workers were insured until 2012 in Guangzhou. Workers not covered by the insurance (such as migrant workers and self-employed workers) tend to have poor working conditions, and this situation may result in an underestimate of heat-related injury risk and economic burden. Thirdly, detailed information such as health status, type of injury, training and job-fit was not available, and future investigation on these would provide a better understanding of heat effects on the work-related injury.

Conclusions

Heat exposure significantly contributed to work-related injuries as well as economic costs in Guangzhou, China. Our findings provide an important quantitative assessment of heat effects on worker's health and insurance payouts, representing a valuable scientific basis for the development of adaptation and mitigation strategies in the light of global warming.

References

1. IPCC, Global warming of 1.5°C. An IPCC Special Report on the impacts of global warming of 1.5°C above pre-industrial levels and related global greenhouse gas emission pathways, in the context of strengthening the global response to the threat of climate change, sustainable development, and efforts to eradicate poverty World Meteorological Organization: Geneva, Switzerland, 2018.
2. Ye, X.; Wolff, R.; Yu, W.; Vaneckova, P.; Pan, X.; Tong, S., Ambient temperature and morbidity: a review of epidemiological evidence. *Environ Health Perspect* **2012**, 120, (1), 19-28.
3. Odame, E. A.; Li, Y.; Zheng, S.; Vaidyanathan, A.; Silver, K., Assessing Heat-Related Mortality Risks among Rural Populations: A Systematic Review and Meta-Analysis of Epidemiological Evidence. *Int J Environ Res Public Health* **2018**, 15, (8).
4. Yu, W.; Mengersen, K.; Wang, X.; Ye, X.; Guo, Y.; Pan, X.; Tong, S., Daily average temperature and mortality among the elderly: a meta-analysis and systematic review of epidemiological evidence. *Int J Biometeorol* **2012**, 56, (4), 569-81.
5. Li, M.; Gu, S.; Bi, P.; Yang, J.; Liu, Q., Heat waves and morbidity: current knowledge and further direction-a comprehensive literature review. *Int J Environ Res Public Health* **2015**, 12, (5), 5256-83.
6. Huang, C.; Barnett, A. G.; Wang, X.; Tong, S., The impact of temperature on years of life lost in Brisbane, Australia. *Nat Clim Change* **2012**, 2, (4), 265-270.
7. Huang, C.; Barnett, A. G.; Wang, X.; Vaneckova, P.; FitzGerald, G.; Tong, S., Projecting future heat-related mortality under climate change scenarios: a systematic review. Environ Health Perspect 2011, 119, (12), 1681-90.
8. Kjellstrom, T.; Briggs, D.; Freyberg, C.; Lemke, B.; Otto, M.; Hyatt, O., Heat, Human Performance, and Occupational Health: A Key Issue for the Assessment of Global Climate Change Impacts. Annu Rev Public Health 2016, 37, 97-112.
9. Schulte, P. A.; Bhattacharya, A.; Butler, C. R.; Chun, H. K.; Jacklitsch, B.; Jacobs, T.; Kiefer, M.; Lincoln, J.; Pendergrass, S.; Shire, J.; Watson, J.; Wagner, G. R., Advancing the framework for considering the effects of climate change on worker safety and health. J Occup Environ Hyg 2016, 13, (11), 847-65.
10. Vanos, J. K.; Warland, J. S.; Gillespie, T. J.; Kenny, N. A., Review of the physiology of human thermal comfort while exercising in urban landscapes and implications for bioclimatic design. Int J Biometeorol 2010, 54, (4), 319-34.
11. Smith, C. J.; Johnson, J. M., Responses to hyperthermia. Optimizing heat dissipation by convection and evaporation: Neural control of skin blood flow and sweating in humans. Auton Neurosci 2016, 196, 25-36.
12. Sheng, R.; Li, C.; Wang, Q.; Yang, L.; Bao, J.; Wang, K.; Ma, R.; Gao, C.; Lin, S.; Zhang, Y.; Bi, P.; Fu, C.; Huang, C., Does hot weather affect work-related injury? A case-crossover study in Guangzhou, China. Int J Hyg Environ Health 2018, 221, (3), 423-428.
13. Kjellstrom, T., Impact of Climate Conditions on Occupational Health and Related Economic Losses: A New Feature of Global and Urban Health in the Context of Climate Change. Asia Pac J Public Health 2016, 28, (2 Suppl), 28S-37S.
14. Mairiaux, P.; Malchaire, J., Workers self-pacing in hot conditions: A case study. Appl Ergon 1985, 16, (2), 85-90.
15. Pilcher, J. J.; Nadler, E.; Busch, C., Effects of hot and cold temperature exposure on performance: a meta-analytic review. Ergonomics 2002, 45, (10), 682-98.
16. Zander, K. K.; Botzen, W. J. W.; Oppermann, E.; Kjellstrom, T.; Garnett, S. T., Heat stress causes substantial labour productivity loss in Australia. Nat Clim Change 2015, 5, (7), 647-651.

17. Xia, Y.; Li, Y.; Guan, D.; Tinoco, D. M.; Xia, J.; Yan, Z.; Yang, J.; Liu, Q.; Huo, H., Assessment of the economic impacts of heat waves: A case study of Nanjing, China. J Clean Prod 2018, 171, 811-819.
18. Xiang, J.; Bi, P.; Pisaniello, D.; Hansen, A.; Sullivan, T., Association between high temperature and work-related injuries in Adelaide, South Australia, 2001-2010. Occup Environ Med 2014, 71, (4), 246-52.
19. Morabito, M.; Cecchi, L.; Crisci, A.; Modesti, P. A.; Orlandini, S., Relationship between work-related accidents and hot weather conditions in Tuscany (central Italy). Ind Health 2006, 44, (3), 458-64.
20. Adam-Poupart, A.; Smargiassi, A.; Busque, M. A.; Duguay, P.; Fournier, M.; Zayed, J.; Labreche, F., Effect of summer outdoor temperatures on work-related injuries in Quebec (Canada). Occup Environ Med 2015, 72, (5), 338-45.
21. Martinez-Solanas, E.; Lopez-Ruiz, M.; Wellenius, G. A.; Gasparrini, A.; Sunyer, J.; Benavides, F. G.; Basagana, X., Evaluation of the Impact of Ambient Temperatures on Occupational Injuries in Spain. Environ Health Perspect 2018, 126, (6), 067002.
22. Xiang, J.; Hansen, A.; Pisaniello, D.; Dear, K.; Bi, P., Correlates of Occupational Heat-Induced Illness Costs: Case Study of South Australia 2000 to 2014. J Occup Environ Med 2018, 60, (9), e463-e469.
23. Ministry of Labor and Social Security of the People's Republic of China; Ministry of Health of the People's Republic of China, GB/T 16180-2006, Standard for identify work ability - Gradation of disability caused by work-related injuries and occupational diseases. In 2006.
24. Otto, M.; Lemke, B.; Kjellstrom, T. Hothaps-Soft: A tool for the estimation and analysis of local climate and population heat exposure; 2014.
25. Bernard, T. E.; Pourmoghani, M., Prediction of workplace wet bulb global temperature. Appl Occup Environ Hyg 1999, 14, (2), 126-34.
26. Takakura, J. y.; Fujimori, S.; Takahashi, K.; Hijioka, Y.; Hasegawa, T.; Honda, Y.; Masui, T., Cost of preventing workplace heat-related illness through worker breaks and the benefit of climate-change mitigation. Environ Res Lett 2017, 12, (6).
27. Xiang, J.; Bi, P.; Pisaniello, D.; Hansen, A., Health impacts of workplace heat exposure: an epidemiological review. Ind Health 2014, 52, (2), 91-101.
28. Kjellstrom, T.; Lemke, B.; Matthias Otto, P.; Hyatt, O. M.; Briggs, D. J.; Freyberg, C. A., Heat Impacts on Work, Human Performance, and Daily Life. In Climate Change and Public Health, 2015; pp 73-86.
29. International Organization for Standardization, ISO 7243:2017, Ergonomics of the thermal environment -- Assessment of heat stress using the WBGT (wet bulb globe temperature) index. In ISO/TC 159/SC 5 Ergonomics of the physical environment: 2017.
30. Lemke, B.; Kjellstrom, T., Calculating workplace WBGT from meteorological data: a tool for climate change assessment. Ind Health 2012, 50, (4), 267-78.
31. Liljegren, J. C.; Carhart, R. A.; Lawday, P.; Tschopp, S.; Sharp, R., Modeling the wet bulb globe temperature using standard meteorological measurements. J Occup Environ Hyg 2008, 5, (10), 645-55.
32. Gasparrini, A.; Armstrong, B.; Kenward, M. G., Distributed lag non-linear models. Stat Med 2010, 29, (21), 2224-34.
33. Gasparrini, A., Distributed Lag Linear and Non-Linear Models in R: The Package dlnm. J Stat Softw 2011, 43, (8), 1-20.
34. R Core Team R: A Language and Environment for Statistical Computing, R Foundation for Statistical Computing: Vienna, Austria, 2018.
35. Minister of Health of the People's Republic of China, GBZ 2.2-2007, Occupational exposure limits for hazardous agents in the workplace. Part2: Physical agents. In 2007.

36. Gasparrini, A.; Leone, M., Attributable risk from distributed lag models. BMC Med Res Methodol 2014, 14, 55.
37. McInnes, J. A.; Akram, M.; MacFarlane, E. M.; Keegel, T.; Sim, M. R.; Smith, P., Association between high ambient temperature and acute work-related injury: a case-crossover analysis using workers' compensation claims data. Scand J Work Env Hea 2017, 43, (1), 86-94.
38. Spector, J. T.; Bonauto, D. K.; Sheppard, L.; Busch-Isaksen, T.; Calkins, M.; Adams, D.; Lieblich, M.; Fenske, R. A., A Case-Crossover Study of Heat Exposure and Injury Risk in Outdoor Agricultural Workers. PLoS One 2016, 11, (10), e0164498.
39. Takala, J.; Hamalainen, P.; Saarela, K. L.; Yun, L. Y.; Manickam, K.; Jin, T. W.; Heng, P.; Tjong, C.; Kheng, L. G.; Lim, S.; Lin, G. S., Global estimates of the burden of injury and illness at work in 2012. J Occup Environ Hyg 2014, 11, (5), 326-37.
40. Pogacar, T.; Casanueva, A.; Kozjek, K.; Ciuha, U.; Mekjavic, I. B.; Kajfez Bogataj, L.; Crepinsek, Z., The effect of hot days on occupational heat stress in the manufacturing industry: implications for workers' well-being and productivity. Int J Biometeorol 2018, 62, (7), 1251-1264.
41. Schwatka, N. V.; Atherly, A.; Dally, M. J.; Fang, H.; v, S. B. C.; Tenney, L.; Goetzel, R. Z.; Jinnett, K.; Witter, R.; Reynolds, S.; McMillen, J.; Newman, L. S., Health risk factors as predictors of workers' compensation claim occurrence and cost. Occup Environ Med 2017, 74, (1), 14-23.
42. Fortune, M. K.; Mustard, C. A.; Etches, J. J.; Chambers, A. G., Work-attributed illness arising from excess heat exposure in Ontario, 2004-2010. Can J Public Health 2013, 104, (5), e420-6.
43. Breslin, F. C.; Smith, P., Age-related differences in work injuries: a multivariate, population-based study. Am J Ind Med 2005, 48, (1), 50-6.
44. Tawatsupa, B.; Yiengprugsawan, V.; Kjellstrom, T.; Berecki-Gisolf, J.; Seubsman, S.-A.; Sleigh, A., Association between Heat Stress and Occupational Injury among Thai Workers: Findings of the Thai Cohort Study. Ind Health 2013, 51, (1), 34-46.
45. Xiang, J.; Bi, P.; Pisaniello, D.; Hansen, A., The impact of heatwaves on workers' health and safety in Adelaide, South Australia. Environ Res 2014, 133, 90-5.
46. Gubernot, D. M.; Anderson, G. B.; Hunting, K. L., The epidemiology of occupational heat exposure in the United States: a review of the literature and assessment of research needs in a changing climate. Int J Biometeorol 2014, 58, (8), 1779-88.
47. Marchetti, E.; Capone, P.; Freda, D., Climate change impact on microclimate of work environment related to occupational health and productivity. Ann Ist Super Sanita 2016, 52, (3), 338-342.
48. Gao, C.; Kuklane, K.; Ostergren, P. O.; Kjellstrom, T., Occupational heat stress assessment and protective strategies in the context of climate change. Int J Biometeorol 2018, 62, (3), 359-371.
49. Marcum, J. L.; Chin, B.; Anderson, N. J.; Bonauto, D. K., Self-Reported Work-Related Injury or Illness - Washington, 2011-2014. MMWR Morb Mortal Wkly Rep 2017, 66, (11), 302-306.
50. Spector, J. T.; Krenz, J.; Blank, K. N., Risk Factors for Heat-Related Illness in Washington Crop Workers. J Agromedicine 2015, 20, (3), 349-59.
51. Foley, M., Factors underlying observed injury rate differences between temporary workers and permanent peers. Am J Ind Med 2017, 60, (10), 841-851.
52. Chau, N.; Mur, J.-M.; Touron, C.; Benamghar, L.; Dehaene, D., Correlates of Occupational Injuries for Various Jobs in Railway Workers: A Case-Control Study. J Occup Health 2004, 46, (4), 272-280.
53. Yu, I. T.; Yu, W.; Li, Z.; Qiu, H.; Wan, S.; Xie, S.; Wang, X., Effectiveness of participatory training in preventing accidental occupational injuries: a randomized-controlled trial in China. Scand J Work Env Hea 2017, (3), 226-233.

54. Chercos, D. H.; Berhanu, D., Work related injury among Saudi Star Agro Industry workers in Gambella region, Ethiopia; a cross-sectional study. J Occup Med Toxicol 2017, 12, 7.
55. Zhao, Y.; Yi, W.; Chan, A. P. C.; Wong, D. P., Impacts of cooling intervention on the heat strain attenuation of construction workers. Int J Biometeorol 2018, 62, (9), 1625-1634.
56. Kjellstrom, T.; Freyberg, C.; Lemke, B.; Otto, M.; Briggs, D., Estimating population heat exposure and impacts on working people in conjunction with climate change. Int J Biometeorol 2018, 62, (3), 291-306.

2.3 Overlooked heat-related morbidity indicator: consequence from increasing ambulance dispatches associated with high ambient temperatures

Yiling He [1], **Cunrui Huang** [1,*]

[1] School of Public Health, Sun Yat-sen University, Guangzhou, China
* Correspondence: huangcr@mail.sysu.edu.cn, School of Public Health, Sun Yat-sen University, Zhongshan Road #2, Guangzhou 510080, China (C.H.)

Abstract:

Background: Heat exposure is known to have a complex set of physiological effects and pose a health threat to the whole population. However, current investigations of heat effects were mostly based on several prespecified health outcomes, and less is known about heat impacts of population morbidity. As the front line of medical services, ambulance dispatches may provide a further understanding of the health impacts of heat in the population scale.

Methods: Daily ambulance dispatches between 2015 and 2016 in Shenzhen were obtained, which include individual characteristics and preliminary diagnoses. We first explored the relationship between daily temperature and ambulance dispatches and set the optimum temperature using distributed nonlinear lag model. Then, stratified analyses by gender, age and a wide range of diagnoses were performed to identify vulnerable subpopulations. We estimated the temperature effect on dispatch by comparing the 95th percentile versus optimum temperature, as determined from the annual time series.

Results: A total of 334,495 ambulance dispatches were reported, with an average daily demand of 458. Significantly rising risk of dispatches was found during heat events (RR= 1.19, 95%CI: 1.11-1.27). The risks generally occurred immediately and lasted for less than 1 day. Both males and females, along with people aged 18–44 and ≥60 years old were susceptible to heat. Highest risk was found for urinary disease (RR=1.75, 95% CI: 1.39-2.20), following 1.41 (95% CI: 1.19-1.67) for alcohol intoxication, 1.24 (95% CI: 1.03-1.50) for obstetric and gynecological disease, 1.23 (95% CI: 1.08-1.41) for dizziness, 1.22 (95% CI: 1.01-1.48) for respiratory disease, 1.19 (95% CI: 1.08-1.31) for traumatic disease, 1.18 (95% CI: 1.01-1.38) for gastrointestinal disease.

Conclusion: We provide new evidence on the heat-related morbidity by using ambulance dispatch as an indicator, especially wider range of susceptible diseases/unreported heat-related diseases, and the significantly vulnerable middle-aged populations. It is important for local communities to develop more target interventions/early warning systems and increase community resilience.

Keywords: Ambient temperature; climate change; ambulance dispatches; human morbidity, vulnerable group

Introduction

As presented in the recent reports, global warming is unequivocal in the 21st century, and consequently, the frequency and duration of heat waves are likely to increase [1-3]. Heat exposure poses various adverse impacts on public health, ranging from well-recognized acute heat illness syndromes, to cardiovascular and respiratory disease, and multiple other syndromes attributed to dehydration [4-6]. Noteworthy effects have been found among the vulnerable groups; they are children, elderly, people with pre-existing diseases, those with low socioeconomic status or living alone [7-11].

Health impacts of heat events were commonly measured by human mortality. Studies have assessed associations with specific categories of death outcomes, such as cardiovascular and respiratory diseases, identifying vulnerabilities among specific populations [12-14]. However, death accounts for a small proportion of heat-related health impacts. Lying at the top of the health effect pyramid, fatal events only representing the extreme impacts. Moreover, as non-fatal events occur before death, it might be more easily prevented by raising public awareness of heat events and promoting advance measures. Hence, non-fatal morbidities should be considered adequately characterizing the health effects of heat stress.

Different from patterns of mortality, most heat-related morbidities was found in heat-related illness, acute renal failure, nephritis, and electrolyte imbalance [15-17]. Currently, sources of morbidity data are primarily hospital-based, mainly concentrated on hospital admissions or emergency department visits. However, using hospital visiting record as the indicator of morbidity may lead to an improper assessment of temperature-health association. For the time of hospital visiting is not the real time of the disease onset, especially for those chronic diseases. In addition, previous research suggested that heat illness presents most commonly to emergency medical services, such as emergency department or ambulance dispatch. The absence of integrated data platform of emergency department visit in most cities, causing difficulties in covering all hospital or emergency department visits for the total population.

Although increases in mortality and morbidity associated with heat exposure have been widely investigated, the complete spectrum of health effects of heat on multiple organ systems in a population scale has not been fully characterized. With high confidence in a projected increase of extreme heat events, and strong association between heat exposures and mortality and morbidity, a thorough understanding of the characteristics of extreme heat impact on human health need to be further explored in order to develop appropriate and effective response strategies. It is key to investigate the impact of stressful heat events on non-fatal events based on population investigation, as the literature is largely lacking in this respect.

Other than hospital-collected morbidity data, ambulance dispatch cases included a comprehensive array of health conditions and were aggregated for each area, could be utilized as a useful source of morbidity. Existing literature has described the rising ambulance dispatches were associated with extreme heat. However, most of these studies were occurred outside China, including the United States [18, 19], Australia [20, 21], Canada [22, 23], Italy [24], and Japan [25, 26]. Only three studies focused on Chinese cities—Shanghai [27], Huainan [28] and Shenzhen [29]. Additionally, less is known about the main health complaints of ambulance dispatches during the heat. Most studies focused on prespecified health conditions, such as heat-related illness or heatstroke, or respiratory and cardiovascular disease, while others only reported total dispatch volume. Thus, a further investigation is needed to assess the heat-related ambulance dispatches, figuring out the characteristics of vulnerable populations with high demands of emergency services during heat events.

We performed a time-series analysis evaluating heat-related ambulance dispatches in Shenzhen, China, with the goal of learning which heat events exacerbate illnesses and lead people to seek medical services, thus proving opportunities for early detection and public education to prevent heat-related illness and death.

Methods

Study area

This study is conducted in Shenzhen, a large city in south China, located approximately 1° south of the Tropic of Cancer, within the Pearl River Delta. The municipality covers an area of 1,997.47 km2. According to the Shenzhen Statistical Yearbook 2017, Shenzhen has a resident population of 11.91 million at the end of 2016 with a high population density of 9,322 per km2. Shenzhen has a subtropical monsoon climate with wet and hot summers and dry and warm winters. According to Meteorological Bureau of Shenzhen Municipality, summer of Shenzhen starts from April and end in November, lasting for 7 months. The long-duration summer significantly affects physical and mental comforts.

Data collection

Ambulance dispatches data

Records of emergency ambulance calls from January 1, 2015 to December 31, 2016 were obtained from the Shenzhen Medical Information Center, recording ambulance dispatches information in the whole city. As ambulance calls contain a large amount of non-business-related calls with no ambulance dispatched, such as butt call, crank call, or calling for cancel the order, we figured out the records with dispatch information into the study object, representing the real need of emergency medical services. Inclusion criteria include cases with recorded information about the time of dispatching from the emergency centre, or time of arriving at the incident places, or information about the personal information or the diagnosis of the patients.

Each case record includes information regarding the date and time of the dispatch, patient's gender and age, cause of the dispatch, and the initial diagnosis. The initial diagnosis describes the primary health concerns identified by the doctors upon their arrival at the incident place, recording the most likely condition of concerns using descriptive text. Dispatches without recorded gender, age or causes were excluded from the stratified analysis.

In this study, we summarized the daily number of ambulance dispatches and stratified by gender, age and causes. We considered four age groups (i.e., <18 years, 18–44 years, 45–59 years, and ≥60 years). Causes were identified through specific keywords of the diagnosis or symptoms. For example, cases with "uric", or "urine", or "urinary", or "renal" were categorized as "urinary disease" group. Categories of "causes" include all causes, two kinds of traumatic disease (including traffic accident injury and non-traffic-accident trauma), eight subcategories of non-trauma diseases, including cardiovascular disease (CVD), mental and behaviour disorder, alcohol intoxication, dizziness, gastrointestinal disease, respiratory disease, obstetric or gynaecological problem, and urinary disease. The emergency department physician checks the classifications of diagnosis.

Meteorological and air pollutant data

We obtained daily meteorological data on minimum, mean and maximum temperatures, and relative humidity from the China Meteorological Data Sharing Service System. The daily mean temperature was selected as the primary exposure index because it better reflects outdoor temperatures that occur throughout the whole day than maximum or minimum temperatures, which occur instantaneously.

Daily air quality data were obtained from the National Urban Air Quality Real-time Publishing Platform (http://106.37.208.233:20035/). The air pollutants in this study included particulate matter with an aerodynamic diameter less than 2.5 μm ($PM_{2.5}$), ozone (O_3), and sulfur dioxide (SO_2).

Statistical analysis

We employed a quasi-Poisson regression using the distributed lag nonlinear model (DLNM) to investigate the effect of temperature on ambulance dispatches, allowing for delayed effects for up to 7 days. Selection of degrees of freedom was based on minimizing Akaike's Information Criterion (AIC) and previous research. Specifically, we used a natural cubic spline with 3 degrees of freedom (dfs) for temperature and a natural cubic spline with 3 dfs for lag to capture the nonlinear temperature effect and the lagged effect. Other potential confounders, including relative humidity with a natural cubic spline of 3 dfs, long-term trend with a natural cubic spline of 7 dfs per year, within-season variation (by month) and day of the week as a categorical variable, and public holidays as a binary variable were controlled.

To assess the heat effect, we set the reference temperature at the optimum reference temperature observed in the risk curve for all ambulance dispatches to secure the comparability among different groups. Heat effect was defined as the relative risk (RR) of the ambulance dispatches for the 95th percentiles of temperature distribution compared with the observed optimum temperature. Gender, age and causes groups were analyse using the stratified analysis.

Sensitivity analysis

We performed sensitivity analyses to examine the robustness of the results. We examined models with the inclusion of same-day $PM_{2.5}$, O_3, and SO_2. In addition, we used daily minimum temperature and daily maximum temperature to replace the daily mean temperature. All statistical analyses were performed using R software version 3.5.1 (packages DLNM).

Results

Data description

Ambulance dispatches distributions by gender, age and diagnosis are summarized in Table 1. A total of 1,308,098 ambulance calls were collected during 2015-2016 in Shenzhen, China. As many as 334,495 calls with dispatching information were selected into study object, amounts to 458 dispatches per day. Among these, 174,975 (52.3%) were male and 102,588 (30.7%) were female, the rest of 17% do not have gender information. The average daily number of ambulance dispatches by age was 25 (5.4%), 228 (49.8%), 66 (14.5%) and 60 (13.2%) for each age group (<18, 18–44, 45–59, and ≥60 years old), the rest of 17.1% were those without age record. Leading causes of ambulance dispatches were traumatic disease (28.7%), cardiovascular disease (9.5%), mental and behaviour disorder (8.7%) and alcohol intoxication (8.6%), while urinary disease accounted least (1.9%). During the study period, the mean average temperature was 25.3°C, and mean relative humidity was 68.5%, reflecting the humid subtropical climate in Shenzhen (supplementary materials Table S1).

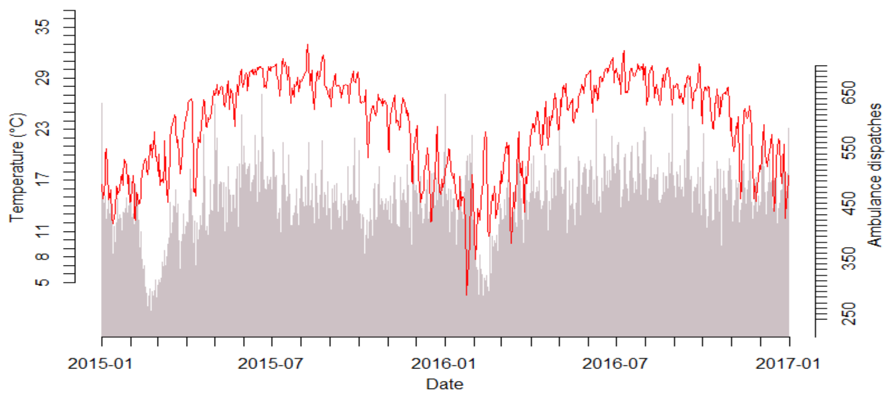


Figure 1. Time-series distribution of daily ambulance dispatches and mean temperature (°C) in Shenzhen, 2015-2016. Red line represents daily mean temperature, and grey regions represent daily ambulance dispatches.

Daily ambulance dispatches and temperature over time are presented in Figure 1, after adjusting for long-term trends and seasonal patterns, relative humidity, day of week and other time-varying confounders. The relationship between mean temperature and ambulance dispatches followed a U-shaped curve (Figure 2). The optimum temperature (OT), corresponding to the lowest point in the exposure-response curve, was 22°C.

Table 1. Descriptive statistics of daily ambulance dispatches in Shenzhen, 2015-2016

Group	Total Dispatches (N)	Daily mean Dispatches (N)	Percentage (%)
All	334 495	458	-
Gender			
Male	174975	239	52.3
Female	102588	140	30.7
Not known	56932	78	17.0
Age (years)			
0-17	17 981	25	5.4
18-44	166 678	228	49.8
45-59	48 423	66	14.5
≥ 60	44 154	60	13.2
Not known	57 259	78	17.1
Diagnosis			
Traumatic disease	113145	155	28.7
Cardiovascular disease	37554	51	9.5
Mental and behavior disorder	34476	47	8.7
Alcohol intoxication	33928	46	8.6
Dizziness	30450	42	7.7
Gastrointestinal disease	19548	27	5.0
Traffic accident	15080	21	3.8
Respiratory disease	14585	20	3.7
Obstetric or gynecological problem	12206	17	3.1
Urinary disease	7391	10	1.9
Unclassifiable or not known	76441	105	19.4

Note: A patient may be diagnosed with more than one disease. Total diagnoses count therefore is greater than the number of patients.

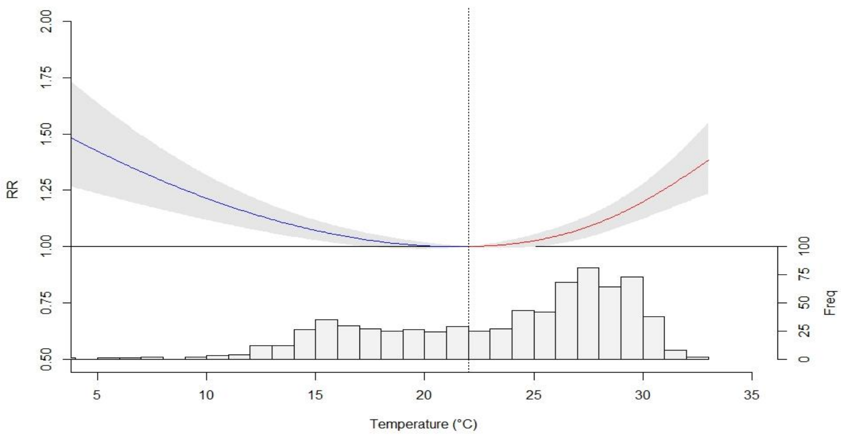


Figure 2. Association between daily mean temperature and ambulance dispatches. The shaded region corresponds to the 95% confidence interval (CI).

Heat-dispatch relationships assessment

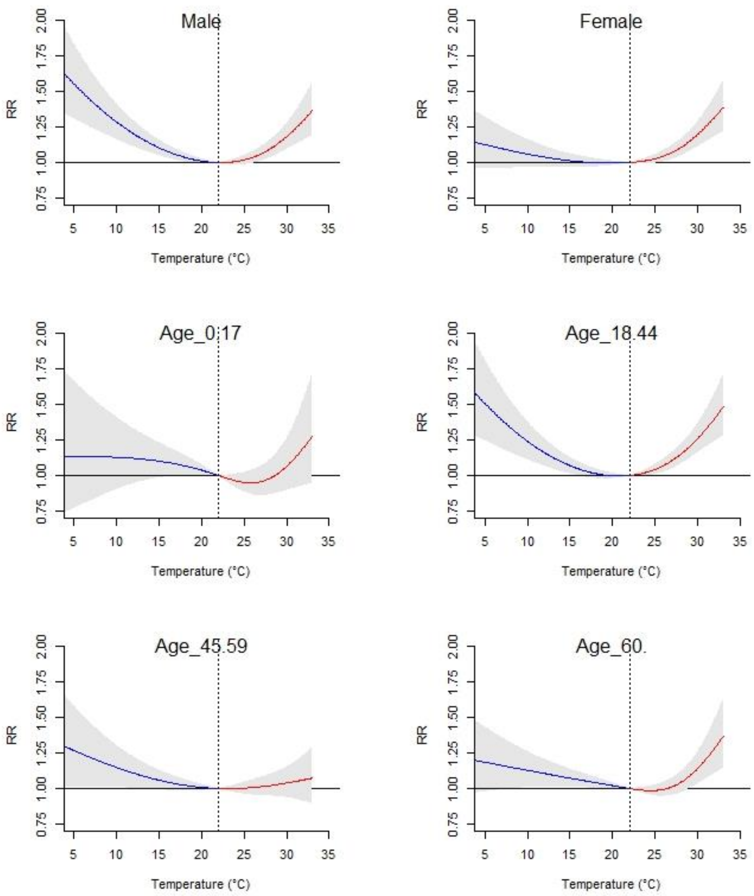


Figure 3. Overall cumulative exposure-response associations between the RRs (95% CI) for ambulance dispatches and daily mean temperature for each gender or age category in Shenzhen, China, 2015-2016

The exposure-response analysis showed significant risk estimates among both males and females, with similar ambulance dispatches-ambient temperature curves

(Figure 3). The overall cumulative RR at the 95th percentile (30.2°C) vs. OT (22°C) was 1.19 (95% CI: 1.10-1.29) for male and 1.21 (95% CI: 1.12-1.30) for female. Ambulance dispatches for the populations aged 18-44 and over 60 years showed significant association with high temperatures (Figure 3). Heat effects were significant and greater in the young people and the elderly, with an RR of 1.27 (95% CI: 1.17-1.39) and 1.15 (95% CI: 1.04-1.28) for people aged 18–44, and ≥60 years old, respectively.

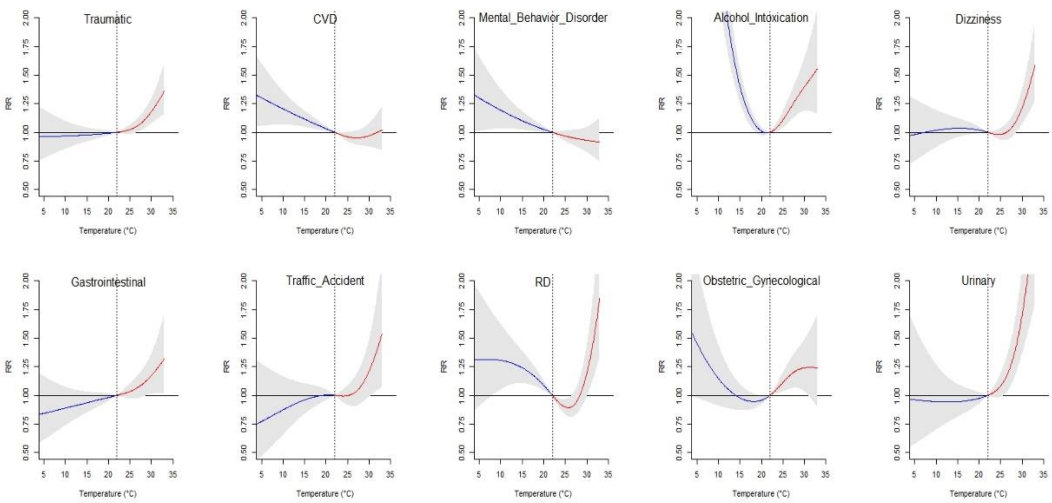
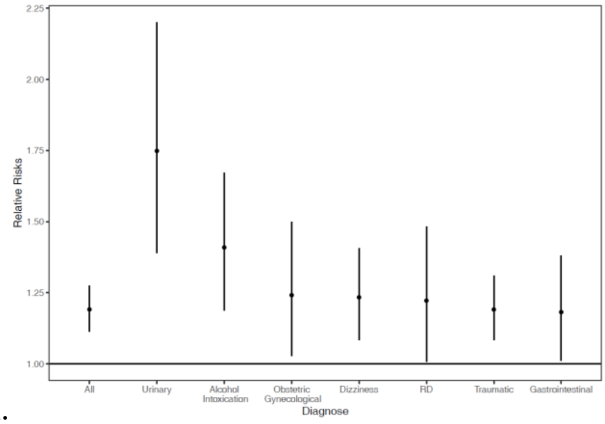


Figure 4. Overall cumulative exposure-response associations between the RRs (95% CI) for ambulance dispatches and daily mean temperature for diseases.

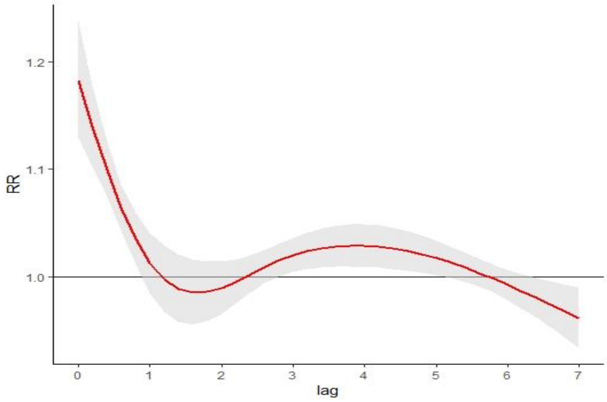
Significant effects of heat were observed among all-cause, non-traffic-accident trauma, alcohol intoxication, dizziness, gastrointestinal disease, traffic accident injury, respiratory disease, obstetric or gynaecological problem, and urinary disease (Figure 4). The cumulative relative risks of ambulance dispatches associated with 95th percentile of temperature (30.2°C) in comparison with OT (22°C) were 1.19 (95%CI: 1.11-1.27) for all-cause, 1.19 (95% CI: 1.08-1.31) for traumatic disease, 1.41 (95% CI: 1.19-1.67) for alcohol intoxication, 1.23 (95% CI: 1.08-1.41) for dizziness, 1.18 (95% CI: 1.01-1.38) for gastrointestinal disease, 1.22 (95% CI: 1.01-1.48) for respiratory disease, 1.24 (95% CI: 1.03-1.50) for obstetric and gynecological disease, 1.75 (95% CI: 1.39-2.20) for urinary disease (Figure 5a). The risk of ambulance dispatches due to heat-sensitive diseases was greatest in the current day of exposure (lag 0) (Figure 5b).

Discussion

This study is the first to systematically assess ambulance dispatches data at a population level, with a wide range of health conditions, by grouping diagnosis into two kinds of traumatic diseases and eight types of non-traumatic diseases. The study contributes to the limited body of literature characterizing changes in human morbidity because of heat exposure. Moreover, it may help to the ongoing characterization of at-risk groups during high-temperature days and development of heat-health watch/warning system.



a.



b.

Figure 5. Relative risks (RRs) for heat-related ambulance dispatches in Shenzhen, 2015-2016. a) RR (and 95% CIs) of ambulance dispatches for all-cause and cause-specific dispatches during extreme heat periods. b) Delayed effect of extreme heat on heat-related ambulance dispatches. Extreme heat was defined as a daily mean temperature exceeding the 95thpercentile (30.2°C) of temperature range.

Emergency ambulance dispatches usually relate to acute health outcomes present earlier to hospitalizations or fatal events. Currently, studies aiming at assessing the adverse effects of heat waves mainly focused on either mortality data or hospital-based data [5, 12, 30, 31]. The findings from these studies may not be extrapolated health outcomes comprehensively or health-seeking behaviours, such as calling for ambulance services. Considering the on-going climate change procedures, heat waves will become more intense, frequent and longer-lasting, posing a wide range of threats to public health. Real-time ambulance dispatches surveillance allows for early detection of residents' medical demands and health status in a region [24]. It is, therefore, necessary to explore the impact of high temperature on ambulance dispatches, and thus providing a broader view of health risks related to extreme heat events.

Effect estimates of high temperature on ambulance dispatches

The adverse and acute effects of high ambient temperature on ambulance dispatches we observed in the present study are consistent with previous studies. For example, Turner et al. found an immediate effect on temperature rise and heatwaves in Brisbane, Australia, and. Also, a nationwide study in Japan suggested a significantly rising risk of ambulance dispatches during extreme heat events [25]. Similar results also found in total ambulance call-outs in Shanghai [27], Huainan [28], and Shenzhen [29] in China.

Previous researches had also compared heat-related ambulance dispatch with hospital admissions and emergency department visits, suggesting that the number of ambulance dispatch and emergency department visits are far greater than hospital admissions [17, 32], and the risky temperature threshold of emergency ambulance dispatches is lower than that of emergency department visits. More sensitive to the heat events, ambulance dispatched therefore considered a good indicator of the occurrence of illness.

A central finding of this study is the high frequency of ambulance dispatches among people aged 18-44 and ≥ 60 years during heat events. This is consistent with previous literature of heat-related mortality or hospital-based morbidity assessment that the elderly were particularly vulnerable to elevated temperatures [33-36]. This may due to their reduced thermoregulatory capacity, underlying chronic disease, together with diminished mobility, that limits their behavioural defences and deteriorates their responses to environment, thus contributing to the heat susceptibility [8, 37].

In our study, however, people aged 18-44 years comprised nearly half of the ambulance dispatch demands and surprisingly suffered the highest risk during heat events. Similar findings were observed in King County, Washington [18], that people aged 15-44 years old had a significant association in emergency medical service calls with high temperatures. The previous study in Shanghai, China also found heat effects on emergency department visits were greater for adults aged <45 years [38].

This is due to young adults having more chances of heat exposure. They may engage in outdoor works, such as agriculture or construction sector, making them exposed to more heat. Moreover, work-related injuries were reported to be heat-related [39, 40]. Accident occurred even though their relatively better capacities for thermoregulation and heat tolerance than the elderly. Another reason might be outdoor activities, such as marathons and jogging, that may further contribute to their susceptible to heat. However, we were unable to assess these potential risk contributors for that ambulance dispatches data does not contain variables describing whether an ambulance demand was related to work or recreational activities. These findings imply that in addition to recognized heat vulnerabilities among those elderly, preventive strategies to protect the health of the young adults during heat events should also be devised.

We found both male and female were sensitive to high temperatures, with similar exposure-response curves. Results were consisted of previous heat-related mortality or morbidity assessment in parts of China [38, 41, 42], while there was no uniform answer to who is more vulnerable during hot days. Males may have more chances of heat exposure due to their outdoor work or activities. While some studies suggest, that females are more heat intolerant than males because of physiological mechanisms according to menopause or pre-existing diseases, such as diabetes [33].

When stratified by health conditions, our results revealed significantly increased risks among six of the non-trauma diseases and both of the traumatic health conditions. This study provides new insight into previously unsuspected possible outcomes associated with heat exposures. Although many of the RR effect estimates of diseases were relatively small, citywide heat exposure may affect a large number population, thus translating to a significant public health burden. With the short lag effect of heat (within 1 day) presents to the ambulance dispatches, this research suggests a need for real-time surveillance or heat-health warning to monitor endangered weather conditions and send appropriate announcements to the public.

Our findings of the rising risks for respiratory diseases, alcohol intoxication, gastrointestinal diseases, and traffic-accident injury during heat events are consistent with existing literature demonstrating an increased risk of mortality and hospital admissions [15, 43]. Increase risks of respiratory diseases and alcohol intoxication have been reported in the limited heat-related ambulance dispatches assessments [18, 25], while other health conditions have not identified in the previous heat-ambulance dispatches literature. This suggests that ambulance dispatches can reflect the health impacts of heat which higher risk in mortality or hospital-collected morbidity were assessed. With wider health outcomes assessed in this study, a better understanding of the relationship between temperatures and ambulance dispatchers was provided.

The estimated exposure-response curves show that some diseases remained unaffected by variations in the mild high apparent temperature, would become highly susceptible when extreme heat events come. Lower risk was found for respiratory disease during mild heat, and then rising sharply when extreme high temperature comes; a similar pattern also found in gastrointestinal diseases and traffic accidents. This might occur due to their adaptive behaviour during hot days, such as staying at home or using air-conditioning to reduce heat exposure. However, when outside temperature increases continually and becomes extremely high, it would be difficult for those to get through. Thus, advance preparedness efforts should be undertaken to allow rapid adaptability when extreme weather events occur.

Our results have revealed a rising risk of urinary disease and obstetric and gynaecological disease, which were consistent with previous hospital-based morbidity, while no evidence was found in the heat-mortality assessment. Rising number of hospital visiting due to urinary tract infections, kidney stone or even renal failure were demonstrated during the heat events [15, 18]. The metabolic evaluation showed that people staying in hot areas presenting more hypocitraturia and low urinary volume [44].

Adverse birth outcomes, such as stillbirth or preterm birth, were proved to be heat-related [45-47]. Though, in present study, birth outcome is unknown when the call received, higher demands of medical services among gestational women during heat events were found. Heat threatens mortality and accelerate the risks of morbidity with a wider range of diseases. To recognized heat vulnerabilities which were commonly reported in mortality research, preventive strategies to protect the health from the non-fatal events should also be devised.

Interestingly, diseases with high rates of mortality and hospitalization during heat events, such as cardiovascular diseases, present a lower risk of ambulance dispatch during hot days. Our result was consistent with previous research of ambulance dispatches, illustrating lower risk of cardiovascular disease during extreme heat events [18, 25]. This may due to insensible fluid losses making volume overload less likely. Also different from prior studies of heat-related morbidity [48, 49], we did not find an association between heat and mental and behaviour disorders. Our finding of inconsistent susceptible diseases among mortality, hospital-based morbidity and ambulance dispatches data suggesting that disease-causing high risks of mortality or hospitalization may not require comparative demands of ambulance services. Since the large demands of ambulance dispatch during heat events, further research on heat-related ambulance dispatch demands characterized by diseases is needed.

The remaining associations revealed in this study – non-accident trauma and dizziness – have received no investigation in the relevant literature, suggesting a wider range of causes for heat-related ambulance dispatches than for hospitalizations or mortality. Previous researches suggest high ambient temperature may increase the work-related injury [39, 40]. This would be the explanation of the increased risk of traumatic problem during hot days since the working-aged people made up the majority of this type of patients. Dizziness in this study includes diagnosis of heatstroke, dizzy and weak, which are non-fatal but acute and could be seriously life-threatening. Considering other recent studies on the effects of heat, our finding indicates that the effects of heat on public health may be captured at an ambulance dispatch level, but not higher up in the public health system.

As the front line of emergency medical service, ambulance dispatchers are greatly affected by emergency events and could reflect the number of population affected by high ambient temperature more accurately. In China, many hospitals can reach its maximum capacity of clinical reception every day. However, ambulance dispatchers are less subject to this influencing factor. Ambulance dispatchers are about several times more numerous than mortality data, representing a wider range of the health effects of heat. In addition, ambulance dispatches may capture potential at-risk population that may not reflect from mortality or admissions data. For example, different from mortality or hospital-based morbidity, working-aged people account for the greatest part of ambulance demands during hot days. And we also find alcohol intoxication and traffic accidents are strongly associated with high ambient temperature which was less investigate in the previous studies, and also no comparable research about the heat impacts on dizziness and injury. This implies that ambulance dispatches data may be useful in surveillance systems as they can be a good indicator of the occurrence of illnesses.

Ambulance attendance could be served for real-time surveillance and heat warning systems. Mortality counts can only be considered reliable after several days, making the mortality-based surveillance system inefficient. However, besides life-threatening diseases, ambulance dispatches can also reflect acute physical discomfort that does not require hospital admission nor cause death, which makes it a good indicator to pick up early signs of temperature effects. Moreover, previous researches suggested the effects of heat on mortality and hospital-based morbidity were highest after the same-day exposure and lasting for 0-3 days. Consistent with previous studies, we found heat effect on ambulance dispatches lasting for no more than one day. This suggests that heat impacts are acute and may occur within several hours after exposure. Given the abundant information recording the time of calling emergency services, ambulance dispatches data may help provide incredible insight into the health impacts of heat, which may help set up real-time heat warning systems and formulate heat response strategies.

Considering ambulance dispatches data record the address of patients were in need of medical services, these can be used to analyze the non-environmental factors that may influence the impacts of heat on health. Local social, economic status and medical resource are suggested to be contributable to the spatial and temporal variations in the effects of high ambient temperature on morbidity and hospitalization [50-52]. This suggests that besides environmental factors, social factors such as social, economic status and medical resource should also be considered to assess the regional sensitivity to temperature, so that can provide valuable evidence to the region-specific policies for emergency medical services and heat-health warning systems.

The results of this study have several important implications for understanding the influence of age regarding vulnerability during heat exposure. Although the elderly were commonly reported more vulnerable in the heat-related mortality assessment, younger people also have high risk for heat-related illness and requires even more emergency ambulance services. The present study suggests that the high risks among middle-aged population may relate to occupational exposure which warrants further study. We can also infer from our results that emergency ambulance services should expect that middle-aged people may take the major part of the ambulance services demands, whereas increases in hospital admission are most likely to be for older patients with multiple chronic conditions.

These findings provide additional information for heat-related health conditions by analyzing a wider range of diseases. Our results may also provide evidence to projections of climate change impacts on public health. To realize this goal, more investigation about the association between temperatures and wider range of health outcomes will be needed in the future study.

A few limitations of this study should also be acknowledged. First, this is a single-city study. Therefore, it is possible that different patterns of heat effect modification by non-environmental factors, such as social demographics and behavioural patterns. Second, heat exposures were measured from meteorological station rather than personal exposure. The temperature difference between indoors and outdoors due to air conditioning or electric fans may lessen the outdoor heat impacts on indoor populations. And the urban heat island effect can also cause temperature varied within a city. Thus, the use of ambient rather than personal exposure measures may not be an accurate reflection of personal real heat exposure. Third, the available diseases coding regime was limited for ambulance attendances; there may lie the risk of misclassification of health outcomes. However, as the primary purpose of the ambulance data set is for administrative and performance evaluation purposes, codes are not required necessarily compared to a hospital setting. Thus, relevant attendance categories were suggested to be grouped.

Conclusions

This study demonstrated a positive association between high temperatures and ambulance dispatches in Shenzhen, China. The high frequency of age-specific effects in middle-aged adults and the elderly, as well as cause-specific effects not previously studied in hospital-based literature, indicate that heat impacts assessment should consider expanding their scope to be more comprehensive.

References

1. (IPCC), I.P.o.C.C., Climate change 2013: the physical science basis. Contribution of Working Group I to the fifth assessment report of the Intergovernmental Panel on Climate Change. 2013, Cambridge and New York: Cambridge University Press.
2. WHO, Protecting health from climate change : World Health Day 2008. 2008, World Health Organization: Geneva.
3. Meehl, G.A. and C. Tebaldi, More intense, more frequent, and longer lasting heat waves in the 21st century. Science, 2004. 305(5686): p. 994-997.
4. Huang, C., A.G. Barnett, X. Wang, and S. Tong, Effects of extreme temperatures on years of life lost for cardiovascular deaths: a time series study in Brisbane, Australia. Circ Cardiovasc Qual Outcomes, 2012. 5(5): p. 609-14.
5. Phung, D., C. Chu, S. Rutherford, H.L.T. Nguyen, C.M. Do, and C. Huang, Heatwave and risk of hospitalization: A multi-province study in Vietnam. Environ Pollut, 2017. 220: p. 597-607.
6. Hajat, S., M. O'Connor, and T. Kosatsky, Health effects of hot weather: from awareness of risk factors to effective health protection. Lancet, 2010. 375(9717): p. 856-63.
7. Phung, D., Y. Guo, H.T.L. Nguyen, S. Rutherford, S. Baum, and C. Chu, High temperature and risk of hospitalizations, and effect modifying potential of socio-economic conditions: A multi-province study in the tropical Mekong Delta Region. Environment International, 2016. 92-93: p. 77-86.
8. Schwartz, J., Who Is Sensitive to Extremes of Temperature? A Case-Only Analysis. Epidemiology, 2005. 16(1): p. 67-72.
9. Anderson, G.B. and L. Bell Michelle, Heat Waves in the United States: Mortality Risk during Heat Waves and Effect Modification by Heat Wave Characteristics in 43 U.S. Communities. Environmental Health Perspectives, 2011. 119(2): p. 210-218.
10. Harlan Sharon, L., H. Declet-Barreto Juan, L. Stefanov William, and B. Petitti Diana, Neighborhood Effects on Heat Deaths: Social and Environmental Predictors of Vulnerability in Maricopa County, Arizona. Environmental Health Perspectives, 2013. 121(2): p. 197-204.
11. Arbuthnott, K.G. and S. Hajat, The health effects of hotter summers and heat waves in the population of the United Kingdom: a review of the evidence. Environ Health, 2017. 16(Suppl 1): p. 119.
12. Huang, C., J. Cheng, D. Phung, B. Tawatsupa, W. Hu, and Z. Xu, Mortality burden attributable to heatwaves in Thailand: A systematic assessment incorporating evidence-based lag structure. Environment International, 2018. 121: p. 41-50.
13. Yin, P., R. Chen, L. Wang, C. Liu, Y. Niu, W. Wang, Y. Jiang, Y. Liu, J. Liu, J. Qi, et al., The added effects of heatwaves on cause-specific mortality: A nationwide analysis in 272 Chinese cities. Environment International, 2018. 121: p. 898-905.
14. Cheng, J., Z. Xu, H. Bambrick, H. Su, S. Tong, and W. Hu, Heatwave and elderly mortality: An evaluation of death burden and health costs considering short-term mortality displacement. Environment International, 2018. 115: p. 334-342.
15. Bobb, J.F., Z. Obermeyer, Y. Wang, and F. Dominici, Cause-specific risk of hospital admission related to extreme heat in older adults. Jama, 2014. 312(24): p. 2659-67.
16. Wilson, L.A., G.G. Morgan, I.C. Hanigan, F.H. Johnston, H. Abu-Rayya, R. Broome, C. Gaskin, and B. Jalaludin, The impact of heat on mortality and morbidity in the Greater Metropolitan Sydney Region: a case crossover analysis. Environ Health, 2013. 12(1): p. 98.
17. Knowlton, K., M. Rotkin-Ellman, G. King, H.G. Margolis, D. Smith, G. Solomon, R. Trent, and P. English, The 2006 California heat wave: impacts on hospitalizations and emergency department visits. Environ Health Perspect, 2009. 117(1): p. 61-7.

18. Calkins, M.M., T.B. Isaksen, B.A. Stubbs, M.G. Yost, and R.A. Fenske, Impacts of extreme heat on emergency medical service calls in King County, Washington, 2007-2012: relative risk and time series analyses of basic and advanced life support. Environ Health, 2016. 15(1): p. 13.
19. Hartz, D.A., A.J. Brazel, and J.S. Golden, A comparative climate analysis of heat-related emergency 911 dispatches: Chicago, Illinois and Phoenix, Arizona USA 2003 to 2006. Int J Biometeorol, 2013. 57(5): p. 669-78.
20. Hansen, A., P. Bi, M. Nitschke, P. Ryan, D. Pisaniello, and G. Tucker, The Effect of Heatwaves on Ambulance Callouts in Adelaide, South Australia. Epidemiology, 2011. 22(1): p. S14-S15.
21. Schaffer, A., D. Muscatello, R. Broome, S. Corbett, and W. Smith, Emergency department visits, ambulance calls, and mortality associated with an exceptional heat wave in Sydney, Australia, 2011: a time-series analysis. Environ Health, 2012. 11(1): p. 3.
22. Dolney, T.J. and S.C. Sheridan, The relationship between extreme heat and ambulance response calls for the city of Toronto, Ontario, Canada. Environ Res, 2006. 101(1): p. 94-103.
23. Bassil, K.L., D.C. Cole, R. Moineddin, W. Lou, A.M. Craig, B. Schwartz, and E. Rea, The relationship between temperature and ambulance response calls for heat-related illness in Toronto, Ontario, 2005. J Epidemiol Community Health, 2011. 65(9): p. 829-31.
24. Alessandrini, E., S. Zauli Sajani, F. Scotto, R. Miglio, S. Marchesi, and P. Lauriola, Emergency ambulance dispatches and apparent temperature: a time series analysis in Emilia-Romagna, Italy. Environ Res, 2011. 111(8): p. 1192-200.
25. Onozuka, D. and A. Hagihara, Spatial and temporal variation in emergency transport during periods of extreme heat in Japan: A nationwide study. Sci Total Environ, 2016. 544: p. 220-9.
26. Kotani, K., K. Ueda, X. Seposo, S. Yasukochi, H. Matsumoto, M. Ono, A. Honda, and H. Takano, Effects of high ambient temperature on ambulance dispatches in different age groups in Fukuoka, Japan. Glob Health Action, 2018. 11(1): p. 1437882.
27. Sun, X., Q. Sun, M. Yang, X. Zhou, X. Li, A. Yu, F. Geng, and Y. Guo, Effects of temperature and heat waves on emergency department visits and emergency ambulance dispatches in Pudong New Area, China: a time series analysis. Environ Health, 2014. 13(1): p. 76.
28. Cheng, J., Z. Xu, D. Zhao, M. Xie, H. Zhang, S. Wang, and H. Su, The burden of extreme heat and heatwave on emergency ambulance dispatches: A time-series study in Huainan, China. Sci Total Environ, 2016. 571: p. 27-33.
29. Zhan, Z.-Y., Y.-M. Yu, J. Qian, Y.-F. Song, P.-Y. Chen, and C.-Q. Ou, Effects of ambient temperature on ambulance emergency call-outs in the subtropical city of Shenzhen, China. PLOS ONE, 2018. 13(11): p. e0207187.
30. Gasparrini, A., Y. Guo, M. Hashizume, E. Lavigne, A. Zanobetti, J. Schwartz, A. Tobias, S. Tong, J. Rocklöv, B. Forsberg, et al., Mortality risk attributable to high and low ambient temperature: a multicountry observational study. The Lancet, 2015. 386(9991): p. 369-375.
31. Tong, S., X.Y. Wang, G. FitzGerald, D. McRae, G. Neville, V. Tippett, P. Aitken, and K. Verrall, Development of health risk-based metrics for defining a heatwave: a time series study in Brisbane, Australia. BMC Public Health, 2014. 14: p. 435.
32. Li, M., S. Gu, P. Bi, J. Yang, and Q. Liu, Heat waves and morbidity: current knowledge and further direction-a comprehensive literature review. Int J Environ Res Public Health, 2015. 12(5): p. 5256-83.
33. Hajat, S., R.S. Kovats, and K. Lachowycz, Heat-related and cold-related deaths in England and Wales: who is at risk? Occupational and Environmental Medicine, 2007. 64(2): p. 93-100.

34. Gronlund Carina, J., A. Zanobetti, D. Schwartz Joel, A. Wellenius Gregory, and S. O'Neill Marie, Heat, Heat Waves, and Hospital Admissions among the Elderly in the United States, 1992–2006. Environmental Health Perspectives, 2014. 122(11): p. 1187-1192.
35. Bai, L., Cirendunzhu, A. Woodward, Dawa, Zhaxisangmu, B. Chen, and Q. Liu, Temperature, hospital admissions and emergency room visits in Lhasa, Tibet: A time-series analysis. Science of The Total Environment, 2014. 490: p. 838-848.
36. Chan, E.Y., W.B. Goggins, J.S. Yue, and P. Lee, Hospital admissions as a function of temperature, other weather phenomena and pollution levels in an urban setting in China. Bull World Health Organ, 2013. 91(8): p. 576-84.
37. Stafoggia, M., F. Forastiere, D. Agostini, N. Caranci, F. de'Donato, M. Demaria, P. Michelozzi, R. Miglio, M. Rognoni, A. Russo, et al., Factors affecting in-hospital heat-related mortality: a multi-city case-crossover analysis. Journal of Epidemiology and Community Health, 2008. 62(3): p. 209-215.
38. Zhang, Y., C. Yan, H. Kan, J. Cao, L. Peng, J. Xu, and W. Wang, Effect of ambient temperature on emergency department visits in Shanghai, China: a time series study. Environ Health, 2014. 13(1): p. 100.
39. Sheng, R., C. Li, Q. Wang, L. Yang, J. Bao, K. Wang, R. Ma, C. Gao, S. Lin, Y. Zhang, et al., Does hot weather affect work-related injury? A case-crossover study in Guangzhou, China. Int J Hyg Environ Health, 2018. 221(3): p. 423-428.
40. Ma, R., S. Zhong, M. Morabito, S. Hajat, Z. Xu, Y. He, J. Bao, R. Sheng, C. Li, C. Fu, et al., Estimation of work-related injury and economic burden attributable to heat stress in Guangzhou, China. Science of The Total Environment, 2019. 666: p. 147-154.
41. Li, Y., Y. Cheng, G. Cui, C. Peng, Y. Xu, Y. Wang, Y. Liu, J. Liu, C. Li, Z. Wu, et al., Association between high temperature and mortality in metropolitan areas of four cities in various climatic zones in China: a time-series study. Environmental health : a global access science source, 2014. 13: p. 65-65.
42. Ban, J., D. Xu, M.Z. He, Q. Sun, C. Chen, W. Wang, P. Zhu, and T. Li, The effect of high temperature on cause-specific mortality: A multi-county analysis in China. Environment International, 2017. 106: p. 19-26.
43. af Wåhlberg, A.E., If you can't take the heat: Influences of temperature on bus accident rates. Safety Science, 2008. 46(1): p. 66-71.
44. Atan, L., C. Andreoni, V. Ortiz, E.K. Silva, R. Pitta, F. Atan, and M. Srougi, High kidney stone risk in men working in steel industry at hot temperatures. Urology, 2005. 65(5): p. 858-861.
45. Strand, L.B., A.G. Barnett, and S. Tong, Maternal Exposure to Ambient Temperature and the Risks of Preterm Birth and Stillbirth in Brisbane, Australia. American Journal of Epidemiology, 2011. 175(2): p. 99-107.
46. Strand, L.B., A.G. Barnett, and S. Tong, The influence of season and ambient temperature on birth outcomes: A review of the epidemiological literature. Environmental Research, 2011. 111(3): p. 451-462.
47. Basu, R., B. Malig, and B. Ostro, High Ambient Temperature and the Risk of Preterm Delivery. American Journal of Epidemiology, 2010. 172(10): p. 1108-1117.
48. Hansen, A., P. Bi, M. Nitschke, P. Ryan, D. Pisaniello, and G. Tucker, The effect of heat waves on mental health in a temperate Australian city. Environmental health perspectives, 2008. 116(10): p. 1369-1375.
49. Chan, E.Y.Y., H.C.Y. Lam, S.H.W. So, W.B. Goggins, J.Y. Ho, S. Liu, and P.P.W. Chung, Association between Ambient Temperatures and Mental Disorder Hospitalizations in a Subtropical City: A Time-Series Study of Hong Kong Special Administrative Region. International journal of environmental research and public health, 2018. 15(4): p. 754.

50. Thach, T.-Q., Q. Zheng, P.-C. Lai, P.P.-Y. Wong, P.Y.-K. Chau, H.J. Jahn, D. Plass, L. Katzschner, A. Kraemer, and C.-M. Wong, Assessing spatial associations between thermal stress and mortality in Hong Kong: A small-area ecological study. Science of The Total Environment, 2015. 502: p. 666-672.
51. Phung, D., C. Chu, D.N. Tran, and C. Huang, Spatial variation of heat-related morbidity: A hierarchical Bayesian analysis in multiple districts of the Mekong Delta Region. Sci Total Environ, 2018. 637-638: p. 1559-1565.
52. Hondula, D.M. and A.G. Barnett, Heat-related morbidity in brisbane, australia: spatial variation and area-level predictors. Environ Health Perspect, 2014. 122(8): p. 831-6.

2.4 Effects of heat on first-ever strokes and the effect modification of atmospheric pressure: A time-series study in Shenzhen, China

Junzhe Bao [1,2,3], Yanfang Guo [4], QiongWang [1,2], Yiling He [1,2], Rui Ma [1,2], Junjie Hua [1,2], Chengsheng Jiang [5], Marco Morabito [6,7], Lin Lei [3], Ji Peng [3,*] and Cunrui Huang [1,2,*]

[1] Department of Health Policy and Management, School of Public Health, Sun Yat-sen University, Guangzhou 510080, China
[2] Guangzhou Key Laboratory of Environmental Pollution and Health Risk Assessment, School of Public Health, Sun Yat-sen University, Guangzhou 510080, China
[3] Shenzhen Center for Chronic Disease Control, Shenzhen 518020, China
[4] Bao'an District Hospital for Chronic Diseases Prevention and Cure, Shenzhen 518100, China
[5] Maryland Institute for Applied Environmental Health, University of Maryland School of Public Health, College Park 20742, MD, USA
[6] Institute of Biometeorology, National Research Council, Florence 50145, Italy
[7] Centre of Bioclimatology, University of Florence, Florence 50144, Italy
[*] Correspondence: pengji126@126.com (J. Peng), huangcr@mail.sysu.edu.cn (C. Huang).

Bao J, Guo Y, Wang Q, He Y, Ma R, Hua J, et al. Effects of heat on first-ever strokes and the effect modification of atmospheric pressure: A time-series study in Shenzhen, China. Science of The Total Environment 2019;654:1372-1378.

Abstract:

Background: Stroke is a leading cause of death globally. Extreme temperatures may induce stroke, but evidence on the effects of heat on first-ever strokes is not clear. Low air pressure can lead to depression and an increase in blood pressure, and it may exacerbate the health impact of heat. In this study, we aimed to evaluate the effects of heat on first-ever strokes, the possible sensitive populations, and the effect of modification of atmospheric pressure.

Methods: We collected data on 142,569 first-ever strokes during 2005–2016 in Shenzhen, a coastal city in southern China, with subtropical oceanic monsoon climate. We fitted a time-series Poisson model in our study, estimating the association between daily mean temperature and first-ever strokes in hot months, with a distributed lag non-linear model with 7 days of lag. We calculated strokes attributable to heat in various gender, age groups, household register types, stroke subtypes, and atmospheric pressure levels.

Results: Heat had a significant cumulative association with first-ever strokes, and the risk of strokes increased with the rise in temperature after it was higher than 30 °C (the 85th percentile). In total, 1.95% (95% empirical CI 0.63–3.20%) of first-ever strokes were attributable to high temperature. The attributable fraction and attributable number of heat were statistically significant in male, female, middle-aged and old patients, immigrant patients, and CBI patients. The fraction attributable to heat was 3.33% in the low atmospheric pressure group, and the number of estimated daily attributable strokes at low atmospheric pressure levels was higher than that of medium and high atmospheric pressure levels ($p<0.01$).

Conclusions: High temperatures in hot months may trigger first-ever strokes, and low atmospheric pressure may exacerbate the effect. We mainly found associations between heat and first-ever strokes for intracerebral haemorrhage, middle-aged and old patients, as well as immigrant patients.

Keywords: Heat; First-ever strokes; Effect modification; Atmospheric pressure; Time-series study

Introduction

Stroke is the second leading cause of death globally, accounting for 5.53 million deaths in 2016, and it is the leading cause of death in China, according to the 2017 disease burden report by Lancet [1]. It is also the second leading disease affecting disability-adjusted life-years (DALYs) throughout the world, and it is the chief disease affecting DALYs in China [2]; it is the 7th leading cause of years lived with disability (YLDs) in China [3]. Strokes largely affect the elderly, and therefore it will become more prominent causes of YLDs in an ageing global population, especially in China. According to a national survey in China, the age-standardized prevalence, incidence, and mortality rates of stroke were 1,114.8/100,000 people, 246.8 and 114.8/100,000 person-years, respectively. Stroke burden in China has increased over the past 30 years[4].

There are 3 primary subtypes of stroke, including ischemic, intracerebral hemorrhagic and subarachnoid hemorrhagic strokes, accounting for 77.8%, 15.8% and 4.4% of all strokes, respectively, while the undetermined type accounted for 2.0%. Hypertension, smoking, alcohol use, obesity, and family history are well-known risk factors for stroke [4, 5]. Also, low and high ambient temperatures can also result in increased risk of stroke mortality and stroke hospital admission [6, 7]. Low temperature may increase blood coagulability and plasma viscosity, while high temperature can influence heart rate, reduce cerebral perfusion and attenuate vasoconstrictor responsiveness; these changes could trigger stroke events [8, 9].

The Intergovernmental Panel on Climate Change (IPCC) reported that the global average temperature increased 0.85 °C (0.65 °C to 1.06 °C) from 1880 to 2012. It is very likely that the number of cold days and nights has decreased and that the number of warm days and nights has increased. There would be an increase in the duration, intensity and spatial extent of heat waves and warm spells during the next decade [10]. Therefore, it is essential to research the influence of heat on stroke.

Most studies investigating the relationship between stroke and temperature focused on stroke mortality, while studies regarding stroke occurrence are lacking [6, 7, 11, 12]. Compared with stroke mortality, stroke morbidity can reflect the early stage of the disease, especially for first-ever strokes. At present, the relationship between heat and first-ever strokes is not clear. Some studies focused on vulnerable patients of stroke facing cold and hot temperatures, while few studies have focused on immigrant populations. At present, increasing numbers of people travel to other cities or countries to work or live, and they may not be able to acclimate to the local climate. Therefore, it is essential to ascertain whether they are sensitive to the adverse weather conditions of their settlements.

Most relevant studies conducted their research at the full-year level and adopted the same time lag for cold and hot when exploring their health effects. However, the adverse influence of low temperature can be delayed and can last for several weeks, while the health effects of high temperature are generally immediate and usually last a week [12-14]. In addition, various factors can modify the effect of temperature on population health, such as humidity [15] and PM10 [16]. However, the effect modification of atmospheric pressure on the heat-stroke relationship is not clear. Previous studies found that low atmospheric pressure could increase the risk of mortality and ischemic stroke [11, 17]. Therefore, it seems plausible that barometric pressure might modify the effect of heat on stroke occurrence.

We aimed to study the influence of heat on first-ever strokes and the relevant sensitive populations, as well as to investigate the effect modification of air pressure, based on 12-year first-ever stroke data from 2005 to 2016. We focused on hot months and conducted our analyses based on the framework of attributable risk assessment within distributed lag non-linear models (DLNMs).

Materials and Methods

Study area

Our study site was Shenzhen, one of the first-tier cities in China. It is a coastal city located within the Pearl River Delta of Guangdong Province, southern China. Shenzhen has a subtropical oceanic monsoon climate, with hot and humid summers, as well as abundant precipitation for most of the year. The average temperature is 28.6 °C in summer. In 2016, there were a total of 11.91 million permanent residents in Shenzhen, 3.85 million (32.33%) of whom had household registration in Shenzhen, and 8.06 million (67.67%) did not. Therefore, most of the residents were from places outside of Shenzhen.

Data collection

First-ever stroke data from January 1, 2005 to December 31, 2016 were collected from the Center for Chronic Disease Control and Prevention in Shenzhen, derived from 69 hospitals in 10 administrative districts (Figure 1), including 142,569 patients. Stroke was defined as "rapidly developed clinical signs of focal disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than of vascular origin" [18]. All the strokes were confirmed by computed tomography (CT) scan or magnetic resonance imaging (MRI) and neurological examination in the hospital. First-ever strokes were those who did not have a history of previous strokes on medical charts and the registration system [19, 20].

Figure 1. The spatial distribution of hospitals included in this study (Shenzhen, China).

All the patients were coded according to the World Health Organization's International Classification of Diseases, the 10th version (ICD-10), ranging from I60 – I64. In our study, all the strokes were classified into 5 subtypes based on the ICD-10 code: (1) subarachnoid haemorrhage (SAH), coded I60; (2) intracerebral haemorrhage (ICH), coded I61; (3) other nontraumatic intracranial hemorrhages (ONIH), coded I62; (4) cerebral infarction (CBI), coded I63; and (5) stroke, not specified as haemorrhage or infarction (SNSHI), coded I64. We primarily focused on CBI and ICH in this study, accounting for 94.66% of all the strokes.

Daily meteorological data were obtained from the National Meteorological Data Sharing Platform (http://data.cma.cn/), including daily mean, maximum and minimum temperature, mean relative humidity, mean wind speed, and atmospheric pressure. Air pollution data during 2014-2016 were obtained from the National Urban Air Quality Real-time Publishing Platform (http://106.37.208.233:20035/) [21].

$$Log[E(Y_t)] = \alpha + \beta Temp_{t,l} + NS(RH_t, 4) + NS(AP_t, 4) + NS(Time, 3 * 12) + \gamma DOW$$

Where Y_t is the observed daily number of strokes at day t, while $E(Y_t)$ is the expected number of strokes at day t; $Temp_{t,l}$ is a cross-basis matrix assessing non-linear and lag effects of daily mean temperature on stroke occurrence over the current day (lag 0) to l days' lag [22], with the lag time set as 7 days, and 4 degrees of freedom (df) for temperatures; NS denotes a natural cubic spline, RH and AP represented daily mean relative humidity and atmospheric pressure, 4 df were used for these variables; Time denotes long-term trends, and we adopted 3 df for each year in this study (only analyzing the hot months) [23]; DOW indicating day of the week. The choice of df for each variable was based on the Akaike information criterion for quasi-Poisson models [24].

Statistical analysis

A distributed lag nonlinear model (dlnm) combined with quasi-Poisson regression was applied with the aim to examine non-linear and lagged effects of heat on first-ever strokes. The analyses were controlled for potential covariates, such as relative humidity, atmospheric pressure, and long-term trends. The model is expressed as follows:

$$Log[E(Y_t)] = \alpha + \beta Temp_{t,l} + NS(RH_t, 4) + NS(AP_t, 4) + NS(Time, 3 * 12) + \gamma DOW$$

Where Y_t is the observed daily number of strokes at day t, while $E(Y_t)$ is the expected number of strokes at day t; $Temp_{t,l}$ is a cross-basis matrix assessing non-linear and lag effects of daily mean temperature on stroke occurrence over the current day (lag 0) to l days' lag [22], with the lag time set as 7 days, and 4 degrees of freedom (df) for temperatures; *NS* denotes a natural cubic spline, *RH* and *AP* represented daily mean relative humidity and atmospheric pressure, 4 df were used for these variables; *Time* denotes long-term trends, and we adopted 3 df for each year in this study (only analyzing the hot months) [23]; *DOW* indicating day of the week. The choice of df for each variable was based on the Akaike information criterion for quasi-Poisson models [24].

We created a seasonal time series data set obtained by restricting to the hot months (June-August) with an addition of an argument called "group" in the cross-basis matrix that broke the series at the end of each group and replaced the first rows up to the maximum lag of the cross-basis matrix in the following series with NA (vignette ("dlnmTS") in the package dlnm).

The minimum-morbidity temperature (MMT), corresponding to the temperature with the minimum stroke occurrence, was derived from the overall temperature–morbidity curve; we found out the MMT value through sourcing a script called "findmin" recently developed by Tobias et al. [25]. We estimated the risk of first strokes attributable to heat based on an approach proposed by Gasparrini et al. [26] and estimated the heat contribution by extracting the association with temperatures higher than the MMT. In addition, we also calculated empirical CI (eCI) using Monte Carlo simulations.

We carried out subgroup analyses to identify the possible sensitive populations to heat by calculating the attributable strokes and fraction of attributable strokes caused by heat (temperatures higher than MMT) in each subgroup. Generally, we focused on various genders, age groups, household register types, and stroke subtypes. We adopted the Cochran Q test in order to test differences between subpopulations [4]. The daily mean air pressure data were divided into 3 subgroups with the aim to identify the effect modification of atmospheric pressure: lower than the 25th percentile of all the data, higher than the 75th percentile and between these two percentiles. We calculated the daily attributable strokes caused by heat, then aggregated the attributable strokes in each subgroup, and further calculated the attributable fraction by dividing the total number of first strokes by the attributable strokes at each atmospheric pressure level [27]. The daily attributable strokes in the group of low air pressure were compared to the attributable strokes in the other 2 groups using the Student's t-test.

We performed sensitivity analyses by changing df values for time trend and relative humidity, also changing the lag days of temperature in the model, as well as adjusting the possible influence of air pollution using the available subset period (during 2014 – 2016). All statistical analyses were computed by using R software (version 3.4.0), with the "dlnm" package (version 2.3.2) to create distributed nonlinear lag models. Two-tailed $P<0.05$ were considered statistically significant.

Results

Table 1. The distribution of demographic characteristics and disease entities of stroke patients

Variables	n	Percent (%)
Gender		
Male	86,709	61
Female	55,860	39
Age (years old)		
<40	11,624	8
40-64	71,493	50
≥65	59,452	42
Household register		
Permanent resident without Hu Ji of Shenzhen*	81,570	57
Permanent resident with Hu Ji of Shenzhen	48,430	34
Transient population	12,569	9
Stroke subtypes		
CBI	104,339	73
ICH	30,656	22
SAH	5,952	4
ONIH	1,253	1
SNSHI	331	0

* Hu Ji is a specific Chinese category; people without Hu Ji of Shenzhen were those who were not born in Shenzhen, while people with Hu Ji of Shenzhen were those who were born in Shenzhen or were working in government agencies, and most of these people were born in Shenzhen.

There were 142,569 first strokes from 2005 to 2016 in Shenzhen, most of them occurring in men (61%), at a mean age of 60 (standard deviation 32) years old, most occurring in persons without Hu Ji of Shenzhen (57%), and most related to cerebral infarction subtype (73%) (Table 1).

The hottest months in Shenzhen were June to August (Figure S1), the mean temperature in these months was 28.6 °C (SD 1.5 °C), and the mean relative humidity and air pressure were 78.2% (SD 7.2%) and 998.7 hPa (SD 36.7 hPa), respectively. The number of daily mean first strokes was 31.6 (SD 15.2) (Table 2).

Table 2. The distribution of daily meteorological factors and daily counts (n) of first strokes during 2005-2016 in hot months

Variable	Mean	SD	Min	25th	50th	75h	Max
Temperature	28.6	1.5	21.7	27.7	28.9	29.7	33.0
Humidity (%)	78.2	7.2	51.0	73.0	78.0	83.0	98.0
Air pressure	998.7	36.7	985.7	996.6	999.1	1001.	1009.9
First strokes (n)	31.6	15.2	4.0	20.0	29.0	41.0	109.0

Correlations between air temperature, barometric pressure and first strokes were statistically significant; high temperature and low air pressure increased the number of first strokes (Table 3).

Table 3. The correlation between meteorological factors and stroke hospitalizations in hot months

Variables	Temperature	Humidity	Air pressure	First strokes
Temperature	1.00			
Humidity	-0.69**	1.00		
Air pressure	-0.02	-0.12**	1.00	
First strokes	0.11**	0.05	-0.089**	1.00

* $p<0.05$; ** $p<0.01$ Spearman correlation analysis was adopted

Figure 2 shows the overall cumulative exposure-response association of first strokes with air temperature over lag 0-7. In general, the temperature-stroke curves were W-shaped: the risk significantly increased with the rise in temperature after it was higher than 27 °C and it decreased after the temperature was higher than 29 °C. The risk then started to increase significantly with the rise in temperature after it was higher than 30 °C.

The effects of heat were more serious for CBI patients than for general stroke patients or ICH patients.

Table 4 shows the estimated attributable fraction (AF) and attributable number (AN) of first strokes caused by heat in various subgroups. AF and AN were 1.95% (95% eCI 0.63-3.20%) and 677 (95% eCI 181-1118) for total strokes, respectively. AF and AN were significant in male, female, middle-aged and old patients, immigrant patients, and CBI patients. The difference of AF between male and female was not statistically significant, as it was the case between middle-aged and old patients ($p>0.05$). The attributable fraction caused by heat was 3.33% in low air pressure conditions; the number of estimated daily attributable strokes at low air pressure levels were higher than that of medium and high air pressure levels ($p<0.01$).

Sensitivity analyses showed that the attributable fractions for total stroke were generally similar using various df for time trend (2-6 df/warm season) and humidity

(2-5 df), using various lag times (3-9 days) in the model, as well as before and after adjusting for various air pollutants (see the supplementary material, Table S1-S3), in this way suggesting the robustness of the analyses.

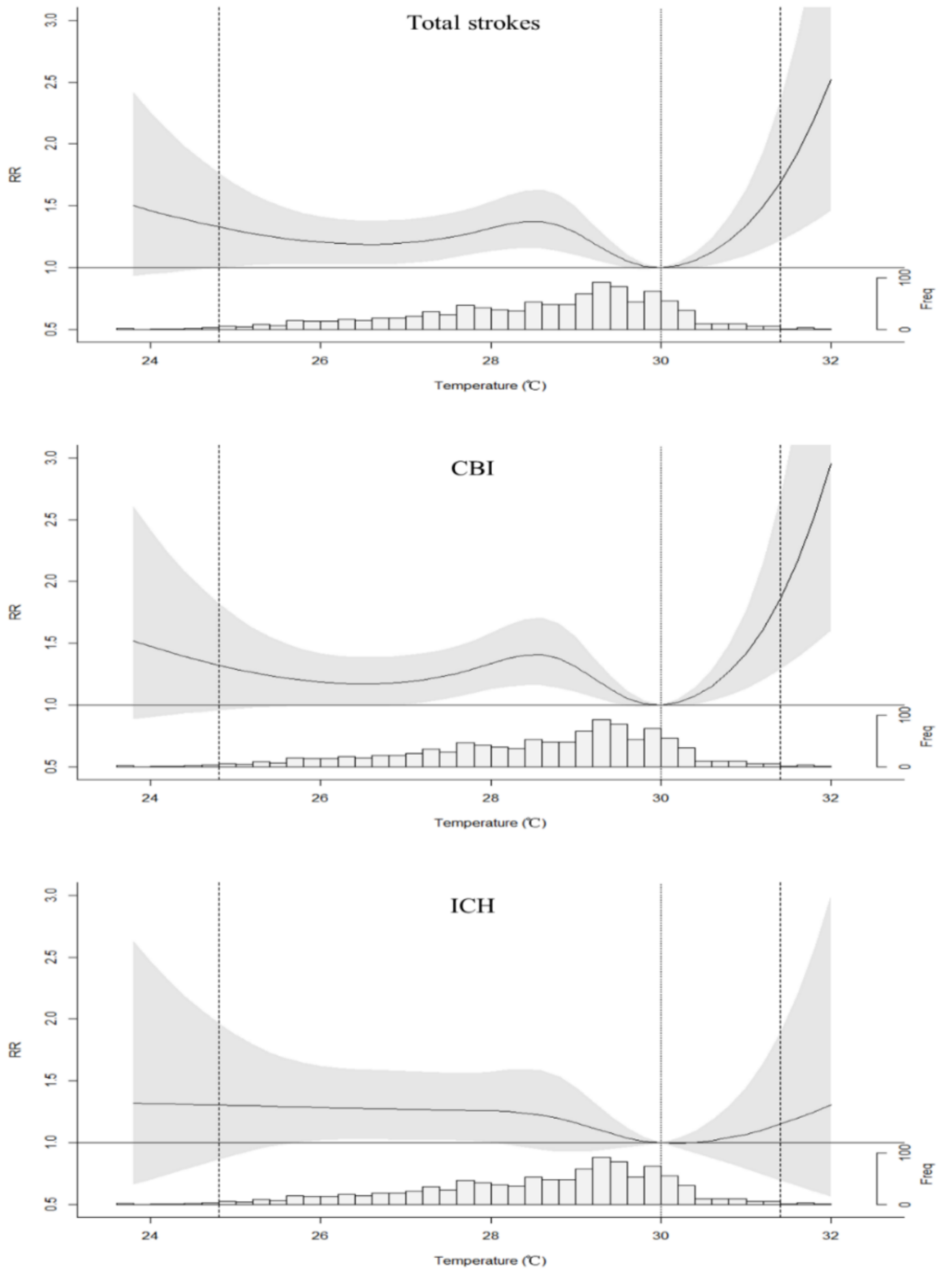


Figure 2. Overall cumulative exposure-response association of first-ever strokes with air temperature during hot months. Upper panel: for total strokes; Middle panel: for CBI subtype; Lower panel: for ICH subtype.

Table 4. The distribution of heat-related attributable fraction (AF, 95% eCI) and attributable number (AN, 95% eCI) in various subgroups of stroke [a]

Variables	AF (%)	95% eCI (%)	AN	95% eCI
Total stroke	1.95	0.63 – 3.20	677	181 - 1118
Gender				
Male	2.04	0.43 – 3.38	431	127 – 699
Female	1.86	0.10 – 3.35	252	27 - 436
Age				
<40	1.65	-0.68 – 3.83	48	-28 - 105
40-64	2.04	0.53 – 3.44	360	102 - 622
≥65	1.87	0.02 - 3.49	266	5 - 476
Household register				
Without Hu Ji Ji	1.96	0.52 - 3.35	391	109 - 647
With Hu Ji	1.87	-0.18 – 3.52	227	-11 - 410
Stroke subtypes category				
CBI	2.32	0.75 – 3.59	610	209 - 975
ICH	0.46	-1.77 - 2.28	31	-104 - 153
Air pressure [b]				
Low	3.33[**]	/	297	/
Medium	1.49	/	267	/
High	1.42	/	111	/

[a] The differences of AF between subpopulations were tested by Cochran Q test.

[b] Classified by the percentiles of the air pressure values (<25%, 25%-75% and >75%).

[**] p<0.01, the daily attributable number of heat in the group of low air pressure was compared to the daily attributable numbers in the other 2 groups.

Discussion

A significant correlation between heat and first strokes was found during hot months by using 12-year first-ever strokes data in Shenzhen. After the daily mean temperature was higher than 30 °C, the risk of first strokes significantly increased with the rise in temperature: the heat accounted for 1.95% (677 cases) of first strokes during hot months. The association between heat and first strokes was found in the stroke subtype of intracerebral haemorrhage, in both male and female patients, in middle-aged and old patients, as well as in immigrant patients. Finally, we explored the effect of modification of air pressure and found that low air pressure strengthened the harmful effects of high temperatures.

We found a W-shaped heat-stroke relationship in this study, and the curve was similar to the results of some other studies [7, 28, 29]. The risk of strokes increased with the rise in daily mean temperatures after they were higher than 27 °C, and the risk decreased after the temperatures were higher than 29 °C. A possible explanation for this phenomenon is that people did not take corresponding measures when the weather became hot (start of the acclimatization phase). Therefore, the health influence of heat was serious at that time; then, as temperatures continued to rise, people might wear less clothing and use air conditioners to adapt to the hot weather (people are acclimated to the heat). When temperatures were higher than 30 °C, the heat became difficult to accommodate and even acclimatized people in the heat can be at risk, especially if they are more vulnerable. However, the W-shaped exposure-response relationship is not common to J-shaped and U-shaped, and the related mechanisms require further researches and validations. The optimum temperature in this study was 30 °C, similar to findings of related studies in Chongqing, Guangzhou, and Bangkok, where summers were hot [7, 26, 30].

Guo et al. [6] studied the effects of ambient temperature on stroke hospital admissions in Guangzhou, a city near Shenzhen, but they did not find a statistically significant harmful effect of hot temperature. A possible explanation is that they set their time lag as long as 21 days, which is suitable for cold temperature but may weaken the effect of heat because the lag time of heat is usually limited to one week. [31]. A study in Beijing also did not find adverse effects of heat on strokes [32]. Conversely, Zhou et al. found that heat significantly increased stroke mortality risks in Jiangsu province, China; they performed their analysis in the warm season (May-September), and set the time lag as 6 days [12]. We also performed whole-year analysis with a time lag set as 21 days and found that the harmful effect of heat was not significant (Figure S2).

Heat can cause failure of thermoregulation and may result in dehydration, salt depletion, and increased surface blood circulation. High temperature may also elevate blood viscosity, cholesterol levels, and sweating thresholds, all of which can lead to stroke [33, 34].

We found that heat can increase the risk of first strokes both in male and female; the values of AF in male was slightly higher compared with female, but the difference between them was not significant. Some studies found that females were more sensitive to heat [7, 12], while a study in Sao Paulo found that males were more vulnerable to heat than females [35]. More male than female patients was found in this study, and the mean male age (58 years old) was younger than that of females (63 years old). Patients included in previous studies prevalently focused on mortality and generally older people than those included in this study. These differences may help to explain different results with previous studies.

Ageing can weaken the immune system, resulting in decreased thermoregulation. In addition, the elderly often suffer from a variety of chronic diseases, including diabetes and hypertension [36]. In the present study, the risk for middle-aged patients was similar to the elderly. A possible explanation is that most of these old people were retired, and they might stay indoors when heat conditions occurred. Therefore, they have similar sensitivity to heat compared with middle-aged people, who needed to work and might have spent more time outdoors in hot weather.

There are many immigrant populations in Shenzhen, coming from various provinces and cities of China, even from other countries. The climate of their hometowns may be strongly different from that of Shenzhen. Therefore, they may not be adapted to the climatic conditions of Shenzhen, such as the hot weather in the summer. Furthermore, the socio-economic status of migrants may be lower than that of local people, resulting in their increasing vulnerability to heat conditions.

We found that CBI was more sensitive to heat than ICH. This situation may be attributable to the pathophysiological differences between the two stroke subtypes. Evaporation and sweating in hot weather may lead to dehydration and electrolyte imbalance, further causing thromboembolism, eventually leading to increased risk of CBI [37, 38]. High temperatures may dilate blood vessels and promote blood pressure decline, eventually reducing the risk of hemorrhagic stroke. A study in Korea also found that high temperature was harmful to ischemic stroke but not for hemorrhagic stroke [39].

Animal experimental models showed that lowering barometric pressure aggravated depression-related behaviours [40]. Barometric pressure was found to be inversely associated with blood pressure and heart rate in rat models [41]. Population-based studies found that lowering barometric pressure might lead to cerebral hypoxia and hypocapnia, as well as to increases in pulse rate in humans [42, 43]. All of these factors may induce strokes. Low atmospheric pressure could also induce spontaneous delivery [44], pulmonary embolism [45], and mental health disorders [46]. A study conducted in Guangzhou, a city close to Shenzhen, found that low air pressure was an important risk factor of mortality [17]. In addition, Morabito et al. also found that the risk of ischemic stroke increased with the decrease of atmospheric pressure [11].

There are several limitations to this study. First, meteorological data were extracted from only one monitoring site rather than from individual exposure measures; the former were not accurate and may have led to measurement errors. Second, the stroke data we analyzed primarily reflected the stroke occurrence of the permanent resident population; the data for the floating population were not complete and accurate, and therefore, our results could not reflect the health effect of heat on the floating population precisely. Third, our research was an ecological study. We found the association between heat and first strokes, but it did not prove causality. Additionally, our findings were based on a single city that had subtropical oceanic monsoon climate, with hot and humid summers. These findings might not be applicable to cities with other climate characteristics.

Conclusions

Heat exposure in summer was associated with the occurrence of first-ever strokes, and the associations were found in the subpopulations of intracerebral haemorrhage, both male and female patients, middle-aged and old patients, as well as immigrant patients. Low atmospheric pressure could enhance the harmful effects of heat on stroke occurrence. The government should take actions to address the health threats of heat against the backdrop of global warming, giving priority to the most sensitive subjects.

References

1. G. B. D. Causes of Death Collaborators, Global, regional, and national age-sex specific mortality for 264 causes of death, 1980-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet 2017, 390, (10100), 1151-1210.
2. DALYs, G. B. D.; Hale Collaborators, Global, regional, and national disability-adjusted life-years (DALYs) for 333 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet* **2017**, 390, (10100), 1260-1344.
3. Disease, G. B. D.; Injury, I.; Prevalence, C., Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet* **2017**, 390, (10100), 1211-1259.
4. Wang, W. Z.; Jiang, B.; Sun, H. X.; Ru, X. J.; Sun, D. L.; Wang, L. H.; Wang, L. M.; Jiang, Y.; Li, Y. C.; Wang, Y. L.; Chen, Z. H.; Wu, S. P.; Zhang, Y. Z.; Wang, D.; Wang, Y. J.; Feigin, V. L.; Investigators, N.-C., Prevalence, Incidence, and Mortality of Stroke in China Results from a Nationwide Population-Based Survey of 480 687 Adults. *Circulation* **2017**, 135, (8), 759-+.
5. Benjamin, E. J.; Virani, S. S.; Callaway, C. W.; Chamberlain, A. M.; Chang, A. R.; Cheng, S.; Chiuve, S. E.; Cushman, M.; Delling, F. N.; Deo, R.; de Ferranti, S. D.; Ferguson, J. F.; Fornage, M.; Gillespie, C.; Isasi, C. R.; Jimenez, M. C.; Jordan, L. C.; Judd, S. E.; Lackland, D.; Lichtman, J. H.; Lisabeth, L.; Liu, S.; Longenecker, C. T.; Lutsey, P. L.; Mackey, J. S.; Matchar, D. B.; Matsushita, K.; Mussolino, M. E.; Nasir, K.; O'Flaherty, M.; Palaniappan, L. P.; Pandey, A.; Pandey, D. K.; Reeves, M. J.; Ritchey, M. D.; Rodriguez, C. J.; Roth, G. A.; Rosamond, W. D.; Sampson, U. K. A.; Satou, G. M.; Shah, S. H.; Spartano, N. L.; Tirschwell, D. L.; Tsao, C. W.; Voeks, J. H.; Willey, J. Z.; Wilkins, J. T.; Wu, J. H.; Alger, H. M.; Wong, S. S.; Muntner, P.; American Heart Association Council on, E.; Prevention Statistics, C.; Stroke Statistics, S., Heart Disease and Stroke Statistics-2018 Update: A Report From the American Heart Association. *Circulation* **2018**, 137, (12), e67-e492.
6. Guo, P.; Zheng, M.; Wang, Y.; Feng, W.; Wu, J.; Deng, C.; Luo, G.; Wang, L.; Pan, B.; Liu, H., Effects of ambient temperature on stroke hospital admissions: Results from a time-series analysis of 104,432 strokes in Guangzhou, China. *Sci Total Environ* **2017**, 580, 307-315.
7. Yang, J.; Yin, P.; Zhou, M.; Ou, C. Q.; Li, M.; Li, J.; Liu, X.; Gao, J.; Liu, Y.; Qin, R.; Xu, L.; Huang, C.; Liu, Q., The burden of stroke mortality attributable to cold and hot ambient temperatures: Epidemiological evidence from China. *Environ Int* **2016**, 92-93, 232-8.
8. Keatinge, W. R.; Coleshaw, S. R.; Easton, J. C.; Cotter, F.; Mattock, M. B.; Chelliah, R., Increased platelet and red cell counts, blood viscosity, and plasma cholesterol levels during heat stress, and mortality from coronary and cerebral thrombosis. *Am J Med* **1986**, 81, (5), 795-800.
9. Woodhouse, P. R.; Khaw, K. T.; Plummer, M.; Foley, A.; Meade, T. W., Seasonal variations of plasma fibrinogen and factor VII activity in the elderly: winter infections and death from cardiovascular disease. *Lancet* **1994**, 343, (8895), 435-9.
10. IPCC, Climate Change 2013: The Physical Science Basis. Contribution of Working Group I to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change. Cambridge University Press: Cambridge, NY, USA, **2013**; p 1535.
11. Morabito, M.; Crisci, A.; Vallorani, R.; Modesti, P. A.; Gensini, G. F.; Orlandini, S., Innovative Approaches Helpful to Enhance Knowledge on Weather-Related Stroke Events Over a Wide Geographical Area and a Large Population. *Stroke* **2011**, 42, (3), 593-600.
12. Zhou, L.; Chen, K.; Chen, X. D.; Jing, Y. S.; Ma, Z. W.; Bi, J.; Kinney, P. L., Heat and mortality for ischemic and hemorrhagic stroke in 12 cities of Jiangsu Province, China. *Sci Total Environ* **2017**, 601, 271-277.

13. Bao, J.; Wang, Z.; Yu, C.; Li, X., The influence of temperature on mortality and its Lag effect: a study in four Chinese cities with different latitudes. *BMC Public Health* **2016**, 16, 375.
14. Wu, W.; Xiao, Y.; Li, G.; Zeng, W.; Lin, H.; Rutherford, S.; Xu, Y.; Luo, Y.; Xu, X.; Chu, C.; Ma, W., Temperature-mortality relationship in four subtropical Chinese cities: a time-series study using a distributed lag non-linear model. *Sci Total Environ* **2013**, 449, 355-62.
15. Zeng, J.; Zhang, X. H.; Yang, J.; Bao, J. Z.; Xiang, H.; Dear, K.; Liu, Q. Y.; Lin, S.; Lawrence, W. R.; Lin, A. H.; Huang, C. R., Humidity May Modify the Relationship between Temperature and Cardiovascular Mortality in Zhejiang Province, China. *Int J Env Res Pub He* **2017**, 14, (11).
16. Luo, K.; Li, R. K.; Wang, Z. S.; Zhang, R. M.; Xu, Q., Effect modification of the association between temperature variability and daily cardiovascular mortality by air pollutants in three Chinese cities. *Environ Pollut* **2017**, 230, 989-999.
17. Ou, C. Q.; Yang, J.; Ou, Q. Q.; Liu, H. Z.; Lin, G. Z.; Chen, P. Y.; Qian, J.; Guo, Y. M., The Impact of Relative Humidity and Atmospheric Pressure on Mortality in Guangzhou, China. *Biomed Environ Sci* **2014**, 27, (12), 917-925.
18. Aho, K.; Harmsen, P.; Hatano, S.; Marquardsen, J.; Smirnov, V. E.; Strasser, T., Cerebrovascular disease in the community: results of a WHO collaborative study. *Bull World Health Organ* **1980**, 58, (1), 113-30.
19. Wang, J.; Ning, X.; Yang, L.; Tu, J.; Gu, H.; Zhan, C.; Zhang, W.; Su, T. C., Sex differences in trends of incidence and mortality of first-ever stroke in rural Tianjin, China, from 1992 to 2012. *Stroke* **2014**, 45, (6), 1626-31.
20. Yamanashi, H.; Ngoc, M. Q.; Huy, T. V.; Suzuki, M.; Tsujino, A.; Toizumi, M.; Takahashi, K.; Thiem, V. D.; Anh, D. D.; Anh, N. T.; Tho le, H.; Maeda, T.; Cox, S. E.; Yoshida, L. M.; Ariyoshi, K., Population-Based Incidence Rates of First-Ever Stroke in Central Vietnam. *PLoS One* **2016**, 11, (8), e0160665.
21. Zheng, Q. W.; Liu, H.; Zhang, J.; Chen, D. F., The effect of ambient particle matters on hospital admissions for cardiac arrhythmia: a multi-city case-crossover study in China. *Environ Health-Glob* **2018**, 17.
22. Gasparrini, A., Distributed Lag Linear and Non-Linear Models in R: The Package dlnm. *J Stat Softw* **2011**, 43, (8), 1-20.
23. Anderson, G. B.; Bell, M. L., Heat waves in the United States: mortality risk during heat **waves** and effect modification by heat wave characteristics in 43 U.S. communities. *Environ Health Perspect* **2011**, 119, (2), 210-8.
24. Guo, Y.; Barnett, A. G.; Pan, X.; Yu, W.; Tong, S., The impact of temperature on mortality in Tianjin, China: a case-crossover design with a distributed lag nonlinear model. *Environ Health Perspect* **2011**, 119, (12), 1719-25.
25. Tobias, A.; Armstrong, B.; Gasparrini, A., Investigating Uncertainty in the Minimum Mortality Temperature Methods and Application to 52 Spanish Cities. *Epidemiology* **2017**, 28, (1), 72-76.
26. Gasparrini, A.; Guo, Y.; Hashizume, M.; Lavigne, E.; Zanobetti, A.; Schwartz, J.; Tobias, A.; Tong, S.; Rocklov, J.; Forsberg, B.; Leone, M.; De Sario, M.; Bell, M. L.; Guo, Y. L.; Wu, C. F.; Kan, H.; Yi, S. M.; de Sousa Zanotti Stagliorio Coelho, M.; Saldiva, P. H.; Honda, Y.; Kim, H.; Armstrong, B., Mortality risk attributable to high and low ambient temperature: a multicountry observational study. *Lancet* **2015**, 386, (9991), 369-75.
27. Yang, J.; Zhou, M.; Ou, C. Q.; Yin, P.; Li, M.; Tong, S.; Gasparrini, A.; Liu, X.; Li, J.; Cao, L.; Wu, H.; Liu, Q., Seasonal variations of temperature-related mortality burden from cardiovascular disease and myocardial infarction in China. *Environ Pollut* **2017**, 224, 400-406.
28. Li, M.; Zhou, M.; Zhang, X.; Huang, J.; Bai, L.; Sang, S.; Zhang, J.; Liu, Q., [Impact of temperature on non-accidental deaths and cause-specific mortality in four districts of Jinan]. *Zhonghua Liu Xing Bing Xue Za Zhi* **2014**, 35, (6), 684-8.

29. Zeng, Q.; Li, G. X.; Cui, Y. S.; Jiang, G. H.; Pan, X. C., Estimating Temperature-Mortality Exposure-Response Relationships and Optimum Ambient Temperature at the Multi-City Level of China. *Int J Env Res Pub He* **2016**, 13, (3).
30. Zhang, Y. S.; Li, S. S.; Pan, X. C.; Tong, S. L.; Jaakkola, J. J. K.; Gasparrini, A.; Guo, Y. M.; Wang, S., The effects of ambient temperature on cerebrovascular mortality: an epidemiologic study in four climatic zones in China. *Environ Health-Glob* **2014**, 13.
31. Yang, J.; Ou, C. Q.; Ding, Y.; Zhou, Y. X.; Chen, P. Y., Daily temperature and mortality: a study of distributed lag non-linear effect and effect modification in Guangzhou. *Environ Health* **2012**, 11, 63.
32. Luo, Y. X.; Li, H. B.; Huang, F. F.; Van Halm-Lutterodt, N.; Xu, Q.; Wang, A. X.; Guo, J.; Tao, L. X.; Li, X.; Liu, M. Y.; Zheng, D. Q.; Chen, S. P.; Zhang, F.; Yang, X. H.; Tan, P.; Wang, W.; Xie, X. Q.; Guo, X. H., The cold effect of ambient temperature on ischemic and hemorrhagic stroke hospital admissions: A large database study in Beijing, China between years 2013 and 2014-Utilizing a distributed lag non-linear analysis. *Environ Pollut* **2018**, 232, 90-96.
33. Bouchama, A.; Knochel, J. P., Heat stroke. *N Engl J Med* **2002**, 346, (25), 1978-88.
34. McGeehin, M. A.; Mirabelli, M., The potential impacts of climate variability and change on temperature-related morbidity and mortality in the United States. *Environ Health Persp* **2001**, 109, 185-189.
35. Bell, M. L.; O'Neill, M. S.; Ranjit, N.; Borja-Aburto, V. H.; Cifuentes, L. A.; Gouveia, N. C., Vulnerability to heat-related mortality in Latin America: a case-crossover study in Sao Paulo, Brazil, Santiago, Chile and Mexico City, Mexico. *Int J Epidemiol* **2008**, 37, (4), 796-804.
36. Kenney, W. L.; Munce, T. A., Invited review: Aging and human temperature regulation. *J Appl Physiol* **2003**, 95, (6), 2598-2603.
37. Rikkert, M. G.; Melis, R. J.; Claassen, J. A., Heat waves and dehydration in the elderly. BMJ 2009, 339, b2663.
38. Schobersberger, W.; Schobersberger, B.; Partsch, H., Travel-related thromboembolism: mechanisms and avoidance. *Expert Rev Cardiovasc Ther* **2009**, 7, (12), 1559-67.
39. Lim, Y. H.; Kim, H.; Hong, Y. C., Variation in mortality of ischemic and hemorrhagic strokes in relation to high temperature. *Int J Biometeorol* **2013**, 57, (1), 145-53.
40. Mizoguchi, H.; Fukaya, K.; Mori, R.; Itoh, M.; Funakubo, M.; Sato, J., Lowering barometric pressure aggravates depression-like behavior in rats. *Behav Brain Res* **2011**, 218, (1), 190-193.
41. Sato, J.; Takanari, K.; Omura, S.; Mizumura, K., Effects of lowering barometric pressure on guarding behavior, heart rate and blood pressure in a rat model of neuropathic pain. *Neurosci Lett* **2001**, 299, (1-2), 17-20.
42. Goldberg, M. S.; Giannetti, N.; Burnett, R. T.; Mayo, N. E.; Valois, M. F.; Brophy, J. M., A panel study in congestive heart failure to estimate the short-term effects from personal factors and environmental conditions on oxygen saturation and pulse rate. *Occup Environ Med* **2008**, 65, (10), 659-66.
43. Tauboll, E.; Sorteberg, W.; Owe, J. O.; Lindegaard, K. F.; Rusten, K.; Sorteberg, A.; Gjerstad, L., Cerebral artery blood velocity in normal subjects during acute decreases in barometric pressure. *Aviat Space Envir Md* **1999**, 70, (7), 692-697.
44. Akutagawa, O.; Nishi, H.; Isaka, K., Spontaneous delivery is related to barometric pressure. *Arch Gynecol Obstet* **2007**, 275, (4), 249-54.
45. Meral, M.; Mirici, A.; Aslan, S.; Akgun, M.; Kaynar, H.; Saglam, L.; Gorguner, M., Barometric pressure and the incidence of pulmonary embolism. *Chest* **2005**, 128, (4), 2190-2194.
46. Schory, T. J.; Piecznski, N.; Nair, S.; El-Mallakh, R. S., Barometric Pressure, Emergency Psychiatric Visits, and Violent Acts. *Can J Psychiat* **2003**, 48, (9), 624-627.

2.5 Interaction of air pollutants and meteorological factors on birth weight in Shenzhen, China

Qiong Wang[a,b], Qianhong Liang[c], Changchang Li[a,b], Meng Ren[a,b], Shao Lin[d], Luke D. Knibbs[e], Huanhuan Zhang[a,b], Wei Gongc, Junzhe Bao[a,b], Suhan Wang[a,b], Xuemei Wang[f], Qingguo Zhaog[h], Cunrui Huang[a,b,*]

[a] Department of Health Policy and Management, School of Public Health, Sun Yat-sen University, Guangzhou, China;

[b] Guangzhou Key Laboratory of Environmental Pollution and Health Risk Assessment, School of Public Health, Sun Yat-sen University, Guangzhou, China;

[c] Department of Ultrasound, Panyu Maternal and Child Care Service Center of Guangzhou, Guangzhou, China;

[d] Department of Epidemiology and Biostatistics, School of Public Health, State University of New York at Albany, Albany, NY;

[e] School of Public Health, The University of Queensland, Herston, Australia;

[f] Institute of Environmental and Climate Research, Jinan University, Guangzhou, China;

[g] Epidemiological Research Office of Key Laboratory of Male Reproduction and Genetics (National Health and Family Planning Commission), Family Planning Research Institute of Guangdong Province, Guangzhou, China;

[h] Epidemiological Research Office of Key Laboratory of Male Reproduction and Genetics (National Health and Family Planning Commission), Family Planning Special Hospital of Guangdong Province, Guangzhou, China

* Correspondence: huangcr@mail.sysu.edu.cn (C.H.)

Wang Q, Liang Q, Li C, Ren M, Lin S, Knibbs L, et al. Interaction of Air Pollutants and Meteorological Factors on Birth Weight in Shenzhen, China. Epidemiology (In press)

Abstract:

Background: This study aimed to assess if air pollutants and meteorological factors synergistically affect birth outcomes in Shenzhen, China.

Methods: A total of 1,206,158 singleton live births between 2005 and 2012 were identified from a birth registry database. Daily average measurements of particulate matter ≤10 μm (PM10), sulfur dioxide (SO2), nitrogen dioxide (NO2), ambient air temperature (T), and dew point temperature (Td), a marker of humidity, were collected. Multivariable logistic regression models were used to evaluate associations between air pollution and small for gestational age (SGA) and full-term low birth weight (TLBW). We classified births into those conceived in the warm (May-October) and cold seasons (November- April) and then estimated interactions between air pollutants and meteorological factors.

Results: An interquartile range (IQR) increase in PM10 exposure during the 1st trimester (23.1 μg/m3) and NO2 during both the 1st and 2nd trimesters (15.1 and 13.4 μg/m3) was associated with SGA and TLBW risk; ORs ranged from 1.01 (95% CI: 1.00-1.02) to 1.09 (1.07-1.12). We observed interactive effects of both air temperature and humidity on PM10 and SGA for newborns conceived in the warm season. Each IQR increase in PM10 (11.1 μg/m3) increased SGA risk by 90% (95% CI: 19-205%) when T<5th percentile, followed by 29% (23-34%) when 5th <T< 95th percentile, and also by 61% (10-38%) when Td<5th percentile and 26% (21-32%) when 5th <Td< 95th percentile.

Conclusions: Our study found evidence of an interactive effect of air temperature and humidity on the association between PM10 exposure and SGA among newborns conceived in the warm season (May-October). Relatively low air temperature or humidity exacerbated the effects of PM10.

Keywords: interaction; air pollution; meteorological factors; small for gestational age; full-term low birth weight

Introduction

Small for gestational age (SGA) and full-term low birth weight (TLBW) are two important indicators reflecting fetal growth restriction. SGA is usually defined as a birth weight less than the 10th percentile of population-based birth weight reference values by gestational age, and TLBW means full-term (≥37 completed gestational weeks) newborns with birth weight <2500g at delivery. Both SGA and TLBW indicate a slow prenatal growth rate. Previous research has suggested that SGA and TLBW are associated with perinatal morbidity and mortality [1], as well as adverse sequelae in later adulthood (e.g. cardiovascular disease and diabetes) [2, 3].

Ambient air pollution can induce systemic inflammation, oxidative stress, and hemodynamic changes, which may lead to impaired oxygen and nutrient transport to the fetus, and in turn, slow fetal growth [4, 5]. A number of studies have reported associations between air pollutant exposure and SGA, TLBW or reduced birth weight [6-19]. However, most of these studies were conducted in areas with relatively low concentrations of air pollution and their findings have been inconsistent. Evidence from areas with higher pollutant concentrations, such as China, is still limited.

The effects of air pollution on birth outcomes could be modified by other factors, including demographic characteristics, maternal co-morbidities, and other environmental exposures. Some studies have found differential effects of air pollution on birth weight by race, infant sex and maternal pre-pregnancy body mass index (BMI) [20, 21]. Recently, studies have suggested that meteorological factors, including temperature and humidity, may be implicated in air pollutants' generation, transport [22-24], and possibly toxicity [25-27]. Zanobetti and Peters [28] highlighted that the health impact associated with exposure to air pollution and weather conditions jointly could be larger than the risk estimates based on air pollution and weather alone. However, previous studies usually evaluated the main effects of air pollution or meteorological factors on birth outcomes separately [29-32], or considered meteorological factors as confounders in the study of air pollution [6-17]; to our knowledge, no published studies have assessed the potential for interactive effects.

In this study, we aimed to investigate the effects of air pollution on adverse birth outcomes, and further explore whether meteorological factors interact with air pollutants to influence these outcomes.

Methods

Study population

The study setting and population has been described previously [33]. In brief, our study population included mothers and their singleton live births in Shenzhen, a megacity in southern China (population ~14.5 million), from January 1, 2005, to December 31, 2012. This represented a total of 1,268,756 mother-child pairs. Information on pregnant women and newborns was collected from the Birth

Registry Database and Maternal and Children's Health Information System in Shenzhen, which covered all midwifery clinics and hospitals in this city.

Variables collected included maternal age, pre-pregnancy BMI, maternal education, number of prenatal examinations, parity, gestational age at birth, date of birth, birth weight, and infant sex. The date of conception was calculated by subtracting the gestational age at birth from the date of birth. According to the average age at menarche (12.76 years) and natural menopausal age (50.76 years) in the Chinese population [34, 35], we excluded pairs with an outlier maternal age from the analyses (<13 or >50 years); this was 17,773 individuals, representing 1.4% of total pairs. Those with missing or outlier gestational age (<20 or >44 weeks) were also excluded (n = 1,394; 0.1%) [33].

Study outcomes

SGA was defined as a newborn with birth weight less than the 10th percentile of population-based birth weight reference for different gestational ages. In this study, a birth weight reference, [36] additionally separated by sex was used. This reference was conducted specifically for the local population of Guangzhou, which is a city adjacent to Shenzhen and which has similar socio-economic characteristics. Since the reference ranges from 26 to 43 gestational weeks, we included the subjects within this range for SGA analyses. TLBW was defined as births delivered at or after 37 weeks, with birth weight less than 2500g. We excluded subjects with missing birth weight (788 pairs, 0.06%).

This study was approved by the medical ethics committee of the School of Public Health, Sun Yat-sen University. Data used in the study were anonymous, and there was no individually identifiable information.

Exposure assessment

Daily 24-hour average air pollution concentrations from the same period were collected from Environmental Monitoring Centers located within Shenzhen city (as shown in Figure 1, 6 monitors from 2005 to 2007; 8 for 2008-2012). Air pollutants (in units of μg/m3) included particulate matter with an aerodynamic diameter ≤ 10 μm (PM10), sulfur dioxide (SO2) and nitrogen dioxide (NO2). Spatiotemporal variability of air pollutants concentrations among monitors is presented in eTable 1 and their correlations in eTable 2. PM10, SO2, and NO2 concentrations varied between the monitors, but overall, they were well correlated (most Pearson's correlation coefficients ranged from 0.6 to 0.9) except for SO2 recorded at the seventh site (coefficients ranged from 0.2 to 0.3 between the seventh and other sites).

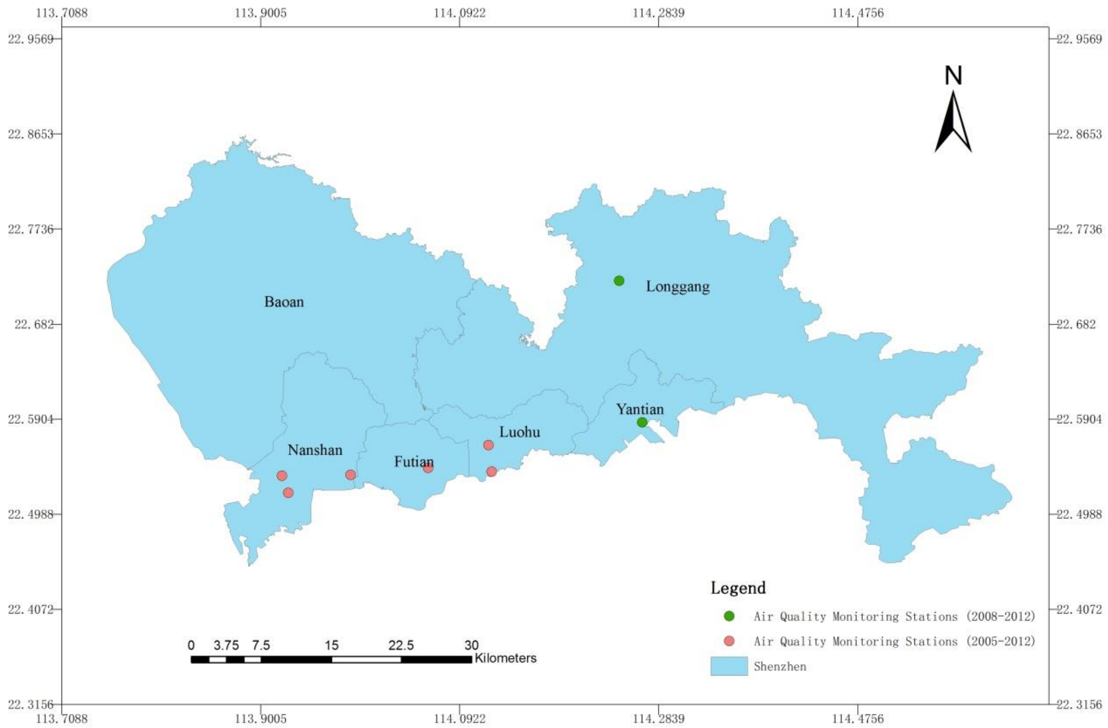


Figure 1. Location of environmental monitoring centres in Shenzhen

Multivariable unconditional logistic regression models were used to calculate the odds ratios (OR) and 95% confidence intervals (CIs) for associations between PM10, NO2 and SO2 (per IQR increase) during each exposure windows (the 1st trimester, 2nd trimester, 3rd trimester, or entire pregnancy) and TLBW. All models were adjusted for covariates, including gestational age, maternal age, maternal education level, parity, season of conception, number of prenatal examinations, pre-pregnancy BMI, and preeclampsia.

To assign air pollution exposure to each subject, we averaged daily PM10, SO2, and NO2 over all monitors and, both with and without the seventh site, and used the estimated date of conception to determine the start and end date of each gestational week for each pregnancy. We then derived the weekly average exposure during each gestational week by averaging the daily mean PM10, SO2, and NO2 for the corresponding seven days. Finally, the weekly exposures were averaged over four exposure windows for each pregnancy: the 1st trimester (gestational week 1 through week 12), 2nd trimester (week 13 to week 27), 3rd trimester (week 28 to birth) and the entire pregnancy (gestational week 1 to birth).

Daily mean temperature (°C) and relative humidity (Rh, %), which were averaged from four measurements taken at 6-hr intervals over each 24-hr period at one meteorological station in Shenzhen, were collected from the Shenzhen Meteorological Bureau. Relative humidity is a routinely reported meteorological factor to the public in China, but it represents the extent to which air is saturated at a given temperature, which may be less informative than other measures of humidity in the context of health studies [37]. Therefore, we used the August-Roche-Magnus approximation [38] to calculate dew point temperature (Td, °C) as a more relevant humidity indicator. We used the same approach to estimate average values for T and Td over four exposure windows for each pregnancy as we did for air pollutants.

Those individuals without exposure information (exposure windows occurring before 2005 when exposure assessment period started, n=42, 6067, 3.4% of total cases) were excluded from final analyses. Among the remaining 1,206,158 births, 1,205,150 births with gestational age from 26 to 43 weeks were used for the SGA analyses, and 1,137,634 births within 37 to 44 weeks were used for TLBW (eTable 3).

Statistical analysis

Pearson's correlation was used to examine the relationship among PM10, SO2, and NO2; they were moderate- to highly- correlated with each other (Table 2). We assessed multicollinearity in a linear model using birth weight as the dependent variable, air pollutants, and covariates including gestational age, maternal age, pre-pregnancy BMI, times of prenatal examination, maternal education levels (≤6, 7-9, 10-12, >12 years), season of conception (spring: March-May; summer: June-August; fall: September-November; winter: December-February), parity (primiparous, multiparous) and preeclampsia as independent variables. We observed variance inflation factor (VIF) < 2 in a single pollutant model which increased to nearly 4 in multi-pollutant models (eTable 4). Multicollinearity may lead to unstable results; we, therefore, did not fit multi-pollutant models and focused instead on single-pollutant models.

Multivariable unconditional logistic regression models were used to calculate the odds ratios (ORs) and 95% confidence intervals (CIs) for associations between PM10, NO2 and SO2 exposure (per IQR increase) during each exposure window (1st, 2nd, and 3rd trimesters, or during the entire pregnancy) and SGA/TLBW, adjusting for the covariates described above.

In sensitivity analyses, we evaluated associations between PM10, NO2 and SO2 exposure during each window and SGA/TLBW using the IQR for the whole gestational period. In order to test if the effects of air pollution varied by delivery method, we evaluated the association between air pollution and SGA/TLBW among vaginal and cesarean births, respectively. We also assessed associations between SO2 and SGA/TLBW after excluding SO2 concentrations recorded at the seventh monitor.

To test the modification effects by meteorological conditions, seasonality should also be taken into account since ambient temperature and humidity have seasonal patterns [29]. Shenzhen has a subtropical oceanic monsoon climate, with high temperatures and precipitation for most of the year, especially from May to October [39]. Therefore, we firstly classified the subjects into those conceived in the warm season (from May to October) and in the cold season (from November to the next April), and then tested for modification of air pollution effects by ambient temperature and humidity within seasons. In order to distinguish relatively extreme conditions, both T and Td were classified using three categories: <5th percentile, 5th -95th percentile, and >95th percentile. We included air pollutants during the whole pregnancy, T or Td (in categories), as well as a cross-product interaction term between them in multivariable unconditional logistic regression models. Wald's method was used to assess interaction on a multiplicative scale. We considered potential evidence of effect modification as an interaction term P-value was less than 0.05. Then, we calculated ORs (and 95% CIs) per IQR increase in PM10, SO2 and NO2 for SGA/TLBW within T and Td categories.

All analyses were performed using SAS version 9.4 (SAS Institute, Inc., Cary, NC).

Results

Of the total births in gestational weeks 26 to 43, 4,480 births had missing infant sex or maternal parity and could not be used to define SGA. Of the remaining 1,200,670 births, 93,574 (7.8%) were SGA. A total of 21,149 (1.9%) were TLBW among 1,137,634 births in gestational weeks 37 to 44.

Distributions of selected characteristics of the subjects are shown in Table 1. Women who delivered SGA babies were more likely to be younger and lighter and attended fewer prenatal examinations. In addition, SGA was observed more frequently among female babies, babies conceived in the cold season (from November to April), from mothers who were less educated, and those with preeclampsia or eclampsia. Distributions of the selected characteristics for TLBW and non-TLBW subjects were similar to SGA and non-SGA subjects, except for parity. SGA was more frequently reported among multiparous women, while TLBW was more frequent among primiparous mothers.

Table 2 shows the summary statistics for PM10, SO2, NO2 during each exposure time window, as well as their correlation. We observed moderate to high positive correlation among PM10, SO2, and NO2 (Pearson's correlation coefficients ranged from 0.5 to 0.8).

We observed that an IQR increase in PM10 (23.1 μg/m3) during the 1st trimester was associated with increased risk of SGA (OR=1.05, 95% CI: 1.04-1.07; Figure 2) and TLBW (OR=1.09, 95% CI: 1.07-1.12; Figure 3). We also found that an IQR increase in PM10 (23.3 μg/m3) during the 2nd trimester and the entire pregnancy (11.1 μg/m3) was associated with TLBW risk. An IQR increase in NO2 during the 1st trimester (15.1 μg/m3) and 2nd trimester (13.4 μg/m3) increased both SGA (the 1st trimester: OR=1.03, 95% CI: 1.02-1.04; the 2nd trimester: OR=1.01, 95% CI: 1.00-1.02; Figure 2) and TLBW risk (the 1st trimester: OR=1.05, 95% CI: 1.02-1.07; the 2nd trimester: OR=1.03, 95% CI: 1.01-1.05; Figure 3). We did not observe positive associations between SO2 exposure and SGA or TLBW during any exposure windows. However, a negative association between SO2 exposure during the entire pregnancy and SGA was found.

Table 1. Distributions of selected characteristics a

Characteristics	SGA	Non-SGA	TLBW	Non-TLBW
Gestational age (years, *Mean±SD*)	38.6±1.8	39±1.6	38.2±1.2	39.2±1.2
Maternal age (years, *Mean±SD*)	26.8±5.0	27.3±4.7	26.7±5.1	27.3±4.7
Pre-pregnancy BMI (Kg/m^2, *Mean±SD*)	19.7±1.9	20.1±2.0	19.7±1.9	20.1±2.0
Number of prenatal examinations (*Mean±SD*)	4.1±3.4	5.0±3.7	4.2±3.4	5.0±3.7
Season of conception (n, %)				
Warm season (May-October)	40702 (43.5)	489326 (44.2)	9214 (43.6)	493215 (44.2)
Cold season (November-April)	52871 (56.5)	617770 (55.8)	11935 (56.4)	623270 (55.8)
Years of education (n, %)				
<=6	5533 (5.9)	45287 (4.1)	1253 (5.9)	46528 (4.2)
7-9	42879 (45.8)	415056 (37.5)	9140 (43.2)	424819 (38.1)
10-12	31895 (34.1)	401223 (36.2)	7325 (34.6)	403254 (36.1)
>12	13266 (14.2)	245530 (22.2)	3431 (16.2)	241884 (21.7)
Parity (n, %)				
Primiparous	53984 (57.7)	677067 (61.2)	14196 (67.1)	674676 (60.4)
Multiparous	39589 (42.3)	430029 (38.8)	6837 (32.3)	437830 (39.2)
Preeclampsia or eclampsia (n, %)				
No	90393 (96.6)	1096340 (99.0)	20132 (95.2)	1106682 (99.1)
Yes	3180 (3.4)	10756 (1.0)	1017 (4.8)	9803 (0.9)
Infant sex (n, %)				
Male	48857 (52.2)	601228 (54.3)	8702 (41.2)	605127 (54.2)
Female	44716 (47.8)	505868 (45.7)	12434 (58.8)	511282 (45.8)

a: SGA: small for gestational age; TLBW: term low birth weight.

Table 2. Pollutant concentration by gestational period and their correlation

Gestational period	Pollutants [a]	Mean	SD	Max	75th	50th	25th	Min	PM_{10}	SO_2	NO_2
1st trimester	PM_{10}	61.2	16.2	135.8	72.6	60.1	49.5	28.7	1.0	0.6	0.8
	NO_2	46.8	10.0	76.3	53.7	45.3	38.6	30.1			1.0
	SO_2	16.2	7.1	35.7	21.5	14.2	10.2	6.4		1.0	0.5
2nd trimester	PM_{10}	58.0	14.6	92.8	69.4	56.3	46.1	32.8	1.0	0.6	0.8
	NO_2	45.5	9.5	75.6	51.2	43.5	37.8	30.4			1.0
	SO_2	15.4	6.9	35.4	19.7	13.6	9.7	6.4		1.0	0.5
3rd trimester	PM_{10}	58.9	15.7	158.8	70.0	57.8	45.8	20.5	1.0	0.6	0.8
	NO_2	45.6	9.7	95.2	51.6	42.9	38.1	21.5			1.0
	SO_2	15.2	6.9	51.5	19.1	13.0	9.8	4.7		1.0	0.5
Entire pregnancy	PM_{10}	59.1	7.0	83.9	64.2	58.5	53.1	40.4	1.0	0.7	0.7
	NO_2	45.9	6.0	66.0	49.8	44.3	42.0	32.5			1.0
	SO_2	15.6	6.4	33.6	20.8	12.9	10.1	7.3		1.0	0.5

[a] Units are microgram per cubic meter (µg/m3) for PM10, SO2 and NO2.

In sensitivity analyses, for an IQR increase in each air pollutant (window specific IQR vs. IQR for the whole gestational period), the associations between air pollution and SGA/TLBW were similar, although the ORs of the latter decreased slightly (eTable 5). When examined by cesarean and vaginal delivery, estimated associations were similar to those based on all live births, with slightly stronger effects observed among cesarean births (eTable 6). By excluding the SO2 concentration recorded at the seventh monitor to assign air pollution exposure, associations between SO2 and SGA/TLBW (eTable 7) were similar to those without the exclusion of the monitor (Figure 2 and Figure 3).

Table 3 shows the summary statistics for T and Td during the whole gestational period by conception season. Pregnant women who conceived in the cold season would experience relatively higher ambient temperature and humidity during their pregnancy, compared with those who conceived in the warm season. Air temperature and dew point temperature were highly correlated in both seasons (Pearson's r = 0.9).

Table 3. Meteorological factors of the entire pregnancy by conception season and their correlation

Meteorological factors [a]	Mean	SD	Max	95th	75th	50th	25th	5th	Min	T	T_d
Conception in warm season (May-October)											
T	22.8	1.1	28.9	24.8	23.5	22.6	22.0	21.2	18.0	1.0	0.9
T_d	15.9	1.3	23.8	18.1	16.7	15.9	15.2	13.9	9.9		1.0
Conception in cold season (November-April)											
T	24.8	1.4	29.1	26.5	26.0	25.3	23.7	22.3	17.2	1.0	0.9
T_d	18.8	1.5	23.2	20.8	19.9	19.2	17.8	16.0	9.6		1.0

[a] T: Air temperature; Td: Dew point temperature; Units are degree Celsius (℃) for air temperature and dew point temperature.

Table 4. Association between air pollution exposure during the entire pregnancy and TLBW/SGA by meteorological factor categories

Air pollutants	Meteorological factor categories [a]			Interaction *P*-value
	<5th percentile OR (95%CI) [b]	5th -95th percentile OR (95%CI) [b]	>95th percentile OR (95%CI) [b]	
Air temperature				
SGA				
PM_{10}	1.90 (1.19-3.05)	1.29 (1.23-1.34)	0.80 (0.57-1.13)	0.001
NO_2	1.29 (1.09-1.53)	1.02 (1.00-1.04)	1.18 (1.07-1.30)	0.17
SO_2	0.91 (0.73-1.14)	0.93 (0.91-0.96)	0.94 (0.78-1.13)	0.05
TLBW				
PM_{10}	2.05 (0.30-14.2)	1.39 (1.27-1.53)	0.60 (0.23-1.58)	0.98
NO_2	0.45 (0.11-1.76)	0.99 (0.94-1.03)	0.94 (0.77-1.15)	0.65
SO_2	0.27 (0.03-2.31)	0.75 (0.69-0.82)	1.96 (0.68-5.63)	0.76
Dew point temperature				
SGA				
PM_{10}	1.61 (1.10-2.38)	1.26 (1.21-1.32)	0.81 (0.58-1.14)	<0.05
NO_2	1.36 (1.15-1.61)	1.02 (1.00-1.04)	1.15 (1.04-1.27)	0.14
SO_2	0.92 (0.59-1.44)	0.80 (0.77-0.83)	1.05 (0.75-1.47)	0.001
TLBW				
PM_{10}	2.53 (0.50-12.74)	1.26 (1.21-1.32)	0.89 (0.63-1.25)	0.43
NO_2	0.43 (0.10-1.80)	0.99 (0.95-1.03)	0.95 (0.77-1.16)	0.57
SO_2	0.76 (0.35-1.61)	0.80 (0.77-0.83)	1.05 (0.75-1.47)	0.21

Conception in warm season: May-October

a: Both air temperature and dew point temperature were classified into three categories: <5th percentile, 5th -95th percentile, and >95th percentile.

b: ORs were calculated for per interquartile increase in each pollutant (11.1 μg/m3 for PM10, 7.8 μg/m3 for NO2, and 10.7 μg/m3 for SO2). All models were adjusted for covariates, including gestational age, maternal age, maternal education level, parity, number of prenatal examinations, pre-pregnancy BMI, and preeclampsia.

As shown in Table 4, we found evidence of interactions between PM10 exposure and air temperature on SGA among the women who conceived in the warm season (Table 4). The association between PM10 exposure and SGA were stronger at relatively low air temperatures compared with higher temperatures (interaction P-value=0.001). Per 11.1 μg/m3 increase in PM10 exposure during the entire pregnancy, SGA risk increased by 90% (95% CI: 19-205%) when T<5th percentile, and by 29% (23-34%) under 'normal' temperatures (5th - 95th percentile). Under relatively high temperatures (T> 95th percentile), no association was observed. We found interactive effects of PM10 and dew point temperature on SGA (interaction P-value<0.05) with similar trends also found for air temperature; SGA risk increased by 61% (10-38%) when Td<5th percentile, and by 26% (21-32%) under 'normal' humidity conditions (5th - 95th percentile). We did not observe any interaction between SO2 exposure and air temperature or dew point temperature on SGA. For TLBW, there were no interactions between any air pollutant and the two meteorological variables. For those conceived in the cold season, there were no associations, nor interactions, between air pollution exposure and TLBW/SGA under different meteorological conditions (eTable 8).

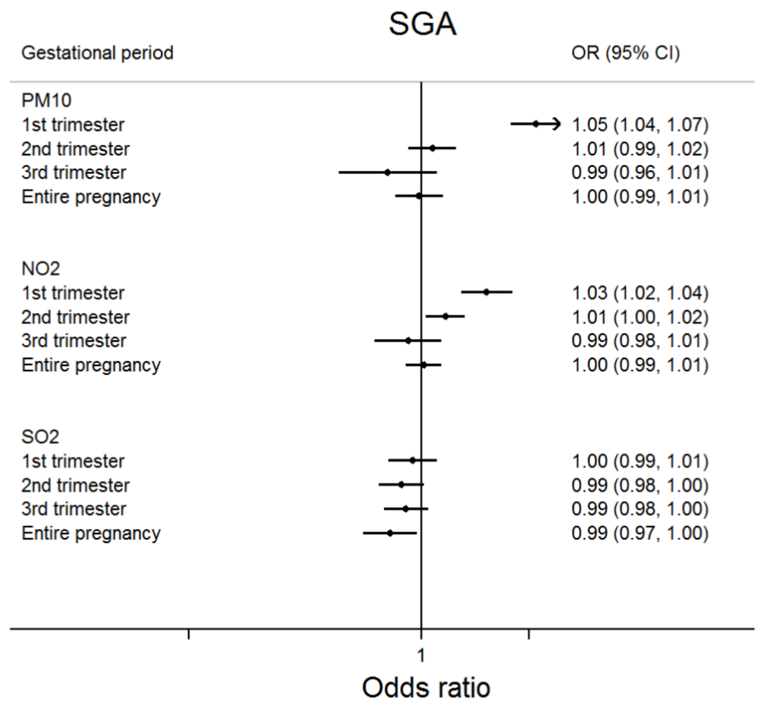


Figure 2. Association between air pollutants and SGA by gestational period

Multivariable unconditional logistic regression models were used to calculate the odds ratios (OR) and 95% confidence intervals (CIs) for associations between PM10, NO2 and SO2 (per IQR increase) during each exposure windows (the 1sttrimester, 2nd trimester, 3rd trimester, or entire pregnancy) and SGA. All models were adjusted for covariates, including gestational age, maternal age, maternal education level, parity, season of conception, number of prenatal examinations, pre-pregnancy BMI, and preeclampsia.

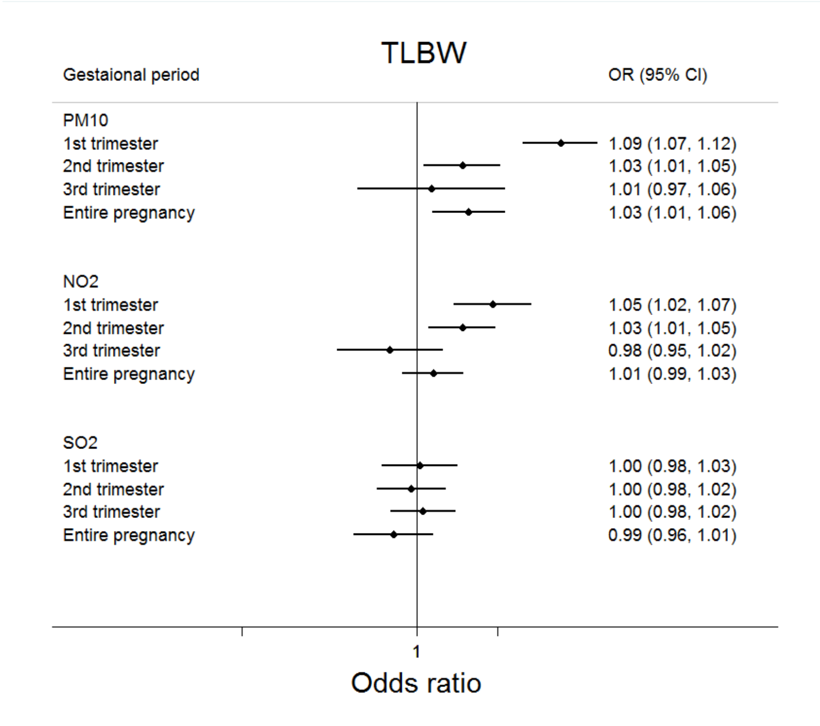


Figure 3. Association between air pollutants and TLBW by gestational period

Discussion

Using a large dataset collected in Shenzhen, a megacity in southern China, ours is the first study that we are aware of to examine the interaction of long-term exposure to air pollution and extreme meteorological factors on adverse birth outcomes. We found that PM10 and NO2 exposures during the 1st and 2nd trimester were associated with increased SGA and TLBW risk. The associations between PM10 exposure during the entire pregnancy and SGA were modified by ambient air temperature and humidity. Relatively low air temperatures or humidity exacerbated the effects of PM10 for the newborns conceived in the warm season (May-October), but not the cold season (November to April).

In this study, the incidence of SGA and TLBW was 7.8% and 1.9%, respectively. TLBW incidence was similar to a previous report based on a nationwide survey in China (2.0%) [40]. Since SGA is usually defined as birth weight less than the 10th percentile of birth weight reference by gestational age, the selection of reference is important for SGA diagnosis. In China, the current nationwide birth weight reference was established in the 1980s [41, 42], which may be outdated since average birth weight has increased recently. A global birth weight reference was established in 2011. However, it only included a limited sample from China (14,286 births) [43]. Dai et al. [44] established a new reference based on a large and nationally-representative database from China; however, this reference value was not stratified by parity, which would affect birth weight [45]. He et al. [36] constructed a new birth weight reference specifically for the local population of Guangzhou separately for gender and parity. Our study population was based in Shenzhen, which is very close to Guangzhou and has similar socio-economic characteristics. Hence, we used the reference value reported by He et al.'s study to define SGA.

Ambient air pollutants can induce oxidative stress, pulmonary and placental inflammation, blood coagulation, as well as endothelial dysfunction and hemodynamic responses [4, 46, 47]. Such changes could affect maternal-placental oxygen and nutrition transport and thus affect fetal growth [4, 46, 47], which, in turn, may result in SGA or TLBW.

In this study, we found that PM10 exposure during the 1st trimester and NO2 during the 1st and 2nd trimester was positively associated with SGA, while SO2 during the entire pregnancy was negatively (but weakly) associated with SGA. Our findings on PM10 and NO2 were consistent with most previous studies conducted overseas [8, 9, 11, 48, 49], although specific trimesters of concern were not consistent across all studies. In a UK cohort, Hannam et al. [8] observed a positive association between PM10 exposure during both the 1st and 3rd trimester, and NO2 exposure during the 3rd trimester, and SGA. The study of Lee et al. [9] in Allegheny County, USA, found 5-8% increases in risk of SGA per IQR (7.7 μg/m3) increase in PM10 exposure during the 1st trimester. Brauer et al. [11] observed that PM10 and NO2 exposure increased the risk of SGA in a Canadian cohort, but they did not observe any particular trimester to be the most important. In Spain, a 10 μg/m3 increase in NO2 during the 2nd trimester was associated with SGA [48]. In Sydney, Australia, Mannes et al. [49] observed NO2 concentrations in the 2nd and 3rd trimesters and one month before birth increased the risk of SGA (ORs between 1.07 and 1.14), and that exposure to PM10 in the 2nd trimester of pregnancy had a small adverse effect on the risk of SGA. However, some other studies [50-52] found no evidence of adverse effects of maternal exposure to PM10, NO2 during pregnancy on SGA.

Compared with PM10 and NO2, few studies have reported associations between SO2 and SGA and their results were mixed, making interpretation difficult. Brauer et al. [11] observed that SO2 exposure increased the risk of SGA with a consistent effect of all exposure windows. Rich et al. study [52] found no association, while we found some negative association between SO2 and SGA.

Compared with SGA, previous studies have paid more attention to low birth weight. Some studies treated birth weight as a continuous variable and found that air pollution increases were associated with decreased birth weight. For instance, Bell et al. found that exposures to PM10 in the 3rd trimester and exposure to NO2 and SO2 in the 1st trimester were associated with lower birth weight by including [21] or excluding preterm births [53]. Other studies also observed associations between maternal PM10 exposure and low birth weight [54, 55]. For categorical birth weight, Pedersen et al. [16] found that PM10 and NO2 exposures during pregnancy were associated with increased risk of TLBW in a European cohort study (ESCAPE): the OR for a 10 μg/m3 increase in PM10 was 1.16 (95% CI: 1.00-1.35) and 1.09 (1.00-1.19) for NO2. Chen et al. study [56] in Brisbane, Australia, found that SO2 and NO2 during the whole pregnancy were associated with increased risk of TLBW, and the highest HRs were observed during the 3rd trimester and the lowest in the 1st trimester. A meta-analysis [57] and a study attempting to implement a standardized study design across 14 populations [58] reported that higher levels of PM10 exposure during pregnancy were associated with increased risk of TLBW.

Our results support and extend previous studies by our observation that exposures to PM10 or NO2 exposure during the 1st trimester and 2nd trimester, as well as PM10 exposure during the whole pregnancy, were associated with TLBW risk. However, other studies [11, 59] did not observe such associations. Moreover, in this study, an association between SO2 and TLBW was not observed, which was inconsistent with a recent review [18], which summarized the association between ambient air pollution and adverse pregnancy outcomes in China and reported that SO2 was associated with LBW. However, they did not separate low birth weight by preterm and term births, which may result in different effects.

Since temperature and humidity can be implicated in air pollutants' generation, transport [22-24], and change personal physiological responses to toxicants [25-27], it may be biologically plausible that ambient temperature or humidity and air pollution interact to affect health outcomes.

In this study, we observed obvious interactions between PM10 exposure and air temperature or humidity among the women who conceived in the warm season. Associations between PM10 exposure and SGA were stronger under relatively low air temperatures. A recent study [56] in Brisbane, Australia also found strengthened effects of PM2.5 exposures in low ambient temperatures on low birth weight. During low ambient temperatures, a pregnant woman's thermoregulatory responses to cold include increased blood viscosity and vascular constriction, which could limit blood flow to the placenta, thereby reducing fetal growth [60]. Given pregnant women who conceived in the warm season would experience relatively low ambient temperatures during their subsequent pregnancy (Table 3), the stronger effects of PM10 exposure we observed for those with very low-temperature exposure within this season (T< 5th percentile), therefore, could be plausible. Relatively low dew point temperature was also observed to exacerbate the effects of PM10 on SGA. Previous studies that addressed this modification of humidity on health effects of air pollution were mostly limited and concentrated on infections [61] or respiratory disease [62, 63], where they observed a lower relative humidity increased the effects of air pollution on health. To the best of our knowledge, no previous studies have focused on birth outcomes. However, since air temperature and dew point temperature are highly correlated in our study (Table 3), we cannot exclude the possibility that interactions between PM10 and the temperature variables may reflect this correlation.

Although the interaction we observed between PM10 exposure and both air temperature and humidity on SGA risk might be biologically plausible [60] and was supported by some evidence from previous studies [56, 62, 63], we interpret the interaction with caution. Since season, air temperature or humidity may be a surrogate for some other unmeasured factors, including O3 [64], constituents of ambient particulate matter, outdoor activities, lifestyle, and biological responses to air pollution [65]. These factors have also been linked to low birth weight [66, 67]. The interactive effects of air pollution and weather on adverse birth outcomes warrants further investigation.

The key strengths of this study are as follows. First, our findings add new evidence on environmental exposure and birth outcomes in a relatively polluted setting. Second, we included more than 1.2 million births from 2005 to 2012 in Shenzhen. The large sample size and long study period likely contributed to increased power to detect associations.

Several limitations should also be mentioned. We used city-wide average air pollutant concentrations, as well as temperature and dew point temperature to assign individual exposure, which may result in exposure misclassification. However, this misclassification is more likely to be non-differential, resulting in attenuation of the associations [68]. In addition, we did not have data on individual level behavioural factors such as exercise and diet, which may confound the associations we observed. However, some previous studies found the effect estimates changed little with and without adjustment for above risk factors [11, 59, 69].

Conclusions

This study examined the interaction of long-term exposure to air pollution and meteorological factors on SGA and TLBW. PM10 and NO2 exposure during the 1st and 2nd trimester was associated with increased SGA and TLBW risk. We observed evidence of an interaction between PM10 exposure during the entire pregnancy and both air temperature and humidity on SGA; the interaction was only apparent for the women who conceived in the warm season (from May to October). Relatively low air temperature and humidity exacerbated the adverse effects of PM10. The results suggest that, in Shenzhen, pregnant women should seek to limit air pollution exposures, particularly during particularly cold or dry days. Air pollution and extreme weather both exert a significant public health burden and their interactive effects warrant further investigation.

References

1. Moraitis, A. A.; Wood, A. M.; Fleming, M.; Smith, G. C., Birth weight percentile and the risk of term perinatal death. Obstet Gynecol 2014, 124, (2 Pt 1), 274-83.
2. Baker, J. L.; Olsen, L. W.; Sorensen, T. I., Weight at birth and all-cause mortality in adulthood. Epidemiology 2008, 19, (2), 197-203.
3. Risnes, K. R.; Vatten, L. J.; Baker, J. L.; Jameson, K.; Sovio, U.; Kajantie, E.; Osler, M.; Morley, R.; Jokela, M.; Painter, R. C.; Sundh, V.; Jacobsen, G. W.; Eriksson, J. G.; Sorensen, T. I.; Bracken, M. B., Birthweight and mortality in adulthood: a systematic review and meta-analysis. International journal of epidemiology 2011, 40, (3), 647-61.
4. Kannan, S.; Misra, D. P.; Dvonch, J. T.; Krishnakumar, A., Exposures to airborne particulate matter and adverse perinatal outcomes: a biologically plausible mechanistic framework for exploring potential effect modification by nutrition. Environmental health perspectives 2006, 114, (11), 1636-42.
5. Schlesinger, R. B.; Kunzli, N.; Hidy, G. M.; Gotschi, T.; Jerrett, M., The health relevance of ambient particulate matter characteristics: coherence of toxicological and epidemiological inferences. Inhalation toxicology 2006, 18, (2), 95-125.
6. Vinikoor-Imler, L. C.; Davis, J. A.; Meyer, R. E.; Messer, L. C.; Luben, T. J., Associations between prenatal exposure to air pollution, small for gestational age, and term low birthweight in a state-wide birth cohort. Environmental research 2014, 132, 132-9.
7. Hyder, A.; Lee, H. J.; Ebisu, K.; Koutrakis, P.; Belanger, K.; Bell, M. L., PM2.5 exposure and birth outcomes: use of satellite- and monitor-based data. Epidemiology 2014, 25, (1), 58-67.
8. Hannam, K.; McNamee, R.; Baker, P.; Sibley, C.; Agius, R., Air pollution exposure and adverse pregnancy outcomes in a large UK birth cohort: use of a novel spatio-temporal modelling technique. Scand J Work Environ Health 2014, 40, (5), 518-30.
9. Lee, P. C.; Roberts, J. M.; Catov, J. M.; Talbott, E. O.; Ritz, B., First trimester exposure to ambient air pollution, pregnancy complications and adverse birth outcomes in Allegheny County, PA. Matern Child Health J 2013, 17, (3), 545-55.
10. van den Hooven, E. H.; Pierik, F. H.; de Kluizenaar, Y.; Hofman, A.; van Ratingen, S. W.; Zandveld, P. Y.; Russcher, H.; Lindemans, J.; Miedema, H. M.; Steegers, E. A.; Jaddoe, V. W., Air pollution exposure and markers of placental growth and function: the generation R study. Environmental health perspectives 2012, 120, (12), 1753-9.
11. Brauer, M.; Lencar, C.; Tamburic, L.; Koehoorn, M.; Demers, P.; Karr, C., A cohort study of traffic-related air pollution impacts on birth outcomes. Environmental health perspectives 2008, 116, (5), 680-6.
12. Huang, C.; Nichols, C.; Liu, Y.; Zhang, Y.; Liu, X.; Gao, S.; Li, Z.; Ren, A., Ambient air pollution and adverse birth outcomes: a natural experiment study. Popul Health Metr 2015, 13, 17.
13. Harris, G.; Thompson, W. D.; Fitzgerald, E.; Wartenberg, D., The association of PM(2.5) with full term low birth weight at different spatial scales. Environmental research 2014, 134, 427-34.
14. Ha, S.; Hu, H.; Roussos-Ross, D.; Haidong, K.; Roth, J.; Xu, X., The effects of air pollution on adverse birth outcomes. Environmental research 2014, 134, 198-204.
15. Basu, R.; Harris, M.; Sie, L.; Malig, B.; Broadwin, R.; Green, R., Effects of fine particulate matter and its constituents on low birth weight among full-term infants in California. Environmental research 2014, 128, 42-51.
16. Pedersen, M.; Giorgis-Allemand, L.; Bernard, C.; Aguilera, I.; Andersen, A. M.; Ballester, F.; Beelen, R. M.; Chatzi, L.; Cirach, M., et al., Ambient air pollution and low birthweight: a European cohort study (ESCAPE). Lancet Respir Med 2013, 1, (9), 695-704.

17. Geer, L. A.; Weedon, J.; Bell, M. L., Ambient air pollution and term birth weight in Texas from 1998 to 2004. J Air Waste Manag Assoc 2012, 62, (11), 1285-95.
18. Jacobs, M.; Zhang, G.; Chen, S.; Mullins, B.; Bell, M.; Jin, L.; Guo, Y.; Huxley, R.; Pereira, G., The association between ambient air pollution and selected adverse pregnancy outcomes in China: A systematic review. The Science of the total environment 2017, 579, 1179-1192.
19. van den Hooven, E. H.; Pierik, F. H.; de Kluizenaar, Y.; Willemsen, S. P.; Hofman, A.; van Ratingen, S. W.; Zandveld, P. Y.; Mackenbach, J. P.; Steegers, E. A.; Miedema, H. M.; Jaddoe, V. W., Air pollution exposure during pregnancy, ultrasound measures of fetal growth, and adverse birth outcomes: a prospective cohort study. Environmental health perspectives 2012, 120, (1), 150-6.
20. Lakshmanan, A.; Chiu, Y. H.; Coull, B. A.; Just, A. C.; Maxwell, S. L.; Schwartz, J.; Gryparis, A.; Kloog, I.; Wright, R. J.; Wright, R. O., Associations between prenatal traffic-related air pollution exposure and birth weight: Modification by sex and maternal pre-pregnancy body mass index. Environmental research 2015, 137, 268-77.
21. Bell, M. L.; Ebisu, K.; Belanger, K., Ambient air pollution and low birth weight in Connecticut and Massachusetts. Environmental health perspectives 2007, 115, (7), 1118-24.
22. Csavina, J.; Field, J.; Felix, O.; Corral-Avitia, A. Y.; Saez, A. E.; Betterton, E. A., Effect of wind speed and relative humidity on atmospheric dust concentrations in semi-arid climates. The Science of the total environment 2014, 487, 82-90.
23. Li, L.; Qian, J.; Ou, C. Q.; Zhou, Y. X.; Guo, C.; Guo, Y., Spatial and temporal analysis of Air Pollution Index and its timescale-dependent relationship with meteorological factors in Guangzhou, China, 2001-2011. Environmental pollution (Barking, Essex : 1987) 2014, 190, 75-81.
24. Tian, G.; Qiao, Z.; Xu, X., Characteristics of particulate matter (PM10) and its relationship with meteorological factors during 2001-2012 in Beijing. Environmental pollution (Barking, Essex : 1987) 2014, 192, 266-74.
25. Gordon, C. J.; Johnstone, A. F.; Aydin, C., Thermal stress and toxicity. Comprehensive Physiology 2014, 4, (3), 995-1016.
26. Leon, L. R., Thermoregulatory responses to environmental toxicants: the interaction of thermal stress and toxicant exposure. Toxicology and applied pharmacology 2008, 233, (1), 146-61.
27. Gordon, C. J., Role of environmental stress in the physiological response to chemical toxicants. Environmental research 2003, 92, (1), 1-7.
28. Zanobetti, A.; Peters, A., Disentangling interactions between atmospheric pollution and weather. Journal of epidemiology and community health 2015, 69, (7), 613-5.
29. Schifano, P.; Lallo, A.; Asta, F.; De Sario, M.; Davoli, M.; Michelozzi, P., Effect of ambient temperature and air pollutants on the risk of preterm birth, Rome 2001-2010. Environment international 2013, 61, 77-87.
30. Arroyo, V.; Diaz, J.; Ortiz, C.; Carmona, R.; Saez, M.; Linares, C., Short term effect of air pollution, noise and heat waves on preterm births in Madrid (Spain). Environmental research 2016, 145, 162-8.
31. Arroyo, V.; Diaz, J.; Carmona, R.; Ortiz, C.; Linares, C., Impact of air pollution and temperature on adverse birth outcomes: Madrid, 2001-2009. Environmental pollution (Barking, Essex : 1987) 2016, 218, 1154-1161.
32. Giorgis-Allemand, L.; Pedersen, M.; Bernard, C.; Aguilera, I.; Beelen, R. M.; Chatzi, L.; Cirach, M.; Danileviciute, A.; Dedele, A., et al., The Influence of Meteorological Factors and Atmospheric Pollutants on the Risk of Preterm Birth. American journal of epidemiology 2017, 185, (4), 247-258.33.
33. Liang, Z.; Lin, Y.; Ma, Y.; Zhang, L.; Zhang, X.; Li, L.; Zhang, S.; Cheng, Y.; Zhou, X.; Lin, H.; Miao, H.; Zhao, Q., The association between ambient temperature and preterm birth in

Shenzhen, China: a distributed lag non-linear time series analysis. Environ Health 2016, 15, (1), 84.
34. Song, Y.; Ma, J.; Hu, P.; Zhang, B., Geographic distribution and secular trend of menarche in 9-18 year-old Chinese Han girls. Journal of Peking University (Health sciences) 2011, 43, (3), 360-364.
35. Shao, H. F.; Sun, D. M.; Liu, J.; Tao, M. F., A survey for reproductive health of postmenopausal women in Shanghai. Journal of Reproductive Medicine 2014, 23, (9), 703-708.
36. He, J. R.; Xia, H. M.; Liu, Y.; Xia, X. Y.; Mo, W. J.; Wang, P.; Cheng, K. K.; Leung, G. M.; Feng, Q.; Schooling, C. M.; Qiu, X., A new birthweight reference in Guangzhou, southern China, and its comparison with the global reference. Arch Dis Child 2014, 99, (12), 1091-7.
37. Davis, R. E.; McGregor, G. R.; Enfield, K. B., Humidity: A review and primer on atmospheric moisture and human health. Environmental research 2016, 144, (Pt A), 106-16.
38. Alduchov, O. A.; Eskridge, R. E., Improved Magnus' form approximation of saturation vapor pressure. J Appl Meteor 1996, 35, 601-609.
39. Broomell, S. B.; Budescu, D. V.; Por, H.-H., Personal experience with climate change predicts intentions to act. Global Environmental Change 2015, 32, (Supplement C), 67-73.
40. Chen, Y.; Li, G.; Ruan, Y.; Zou, L.; Wang, X.; Zhang, W., An epidemiological survey on low birth weight infants in China and analysis of outcomes of full-term low birth weight infants. BMC Pregnancy Childbirth 2013, 13, 242.
41. Zhang, B.; Feng, Z.; Zhang, L., An investigation on the physical development of neonates of various gestational age in 15 cities in China. Chin J Pediatr 1988, 26, 206-208. In Chinese.
42. Zhang, B., Revised report of birth weight of newborns by gestational age for male and female in 15 cities of China. Chin J Pract Pediatr 1992, 7, 306-307. In Chinese.
43. Mikolajczyk, R. T.; Zhang, J.; Betran, A. P.; Souza, J. P.; Mori, R.; Gulmezoglu, A. M.; Merialdi, M., A global reference for fetal-weight and birthweight percentiles. Lancet 2011, 377, (9780), 1855-61.
44. Dai, L.; Deng, C.; Li, Y.; Zhu, J.; Mu, Y.; Deng, Y.; Mao, M.; Wang, Y.; Li, Q.; Ma, S.; Ma, X.; Zhang, Y., Birth weight reference percentiles for Chinese. PloS one 2014, 9, (8), e104779.
45. Lam, D., How the world survived the population bomb: lessons from 50 years of extraordinary demographic history. Demography 2011, 48, (4), 1231-62.
46. Kannan, S.; Misra, D. P.; Dvonch, J. T.; Krishnakumar, A., Exposures to airborne particulate matter and adverse perinatal outcomes: a biologically plausible mechanistic framework for exploring potential. Cien Saude Colet 2007, 12, (6), 1591-602.
47. Erickson, A. C.; Arbour, L., The shared pathoetiological effects of particulate air pollution and the social environment on fetal-placental development. J Environ Public Health 2014, 2014, 901017.
48. Ballester, F.; Estarlich, M.; Iñiguez, C.; Llop, S.; Ramón, R.; Esplugues, A.; Lacasaña, M.; Rebagliato, M., Air pollution exposure during pregnancy and reduced birth size: a prospective birth cohort study in Valencia, Spain. Environmental Health 2010, 9, (1), 6.
49. Mannes, T.; Jalaludin, B.; Morgan, G.; Lincoln, D.; Sheppeard, V.; Corbett, S., Impact of ambient air pollution on birth weight in Sydney, Australia. Occupational and Environmental Medicine 2005, 62, (8), 524-530.
50. Gehring, U.; Van Eijsden, M.; Dijkema, M. B.; Van der Wal, M. F.; Fischer, P.; Brunekreef, B., Traffic-related air pollution and pregnancy outcomes in the Dutch ABCD birth cohort study. Occupational and environmental medicine 2010, oem. 2009.053132.
51. Hansen, C.; Neller, A.; Williams, G.; Simpson, R., Low levels of ambient air pollution during pregnancy and fetal growth among term neonates in Brisbane, Australia. Environmental research 2007, 103, (3), 383-389.

52. Rich, D. Q.; Demissie, K.; Lu, S.-E.; Kamat, L.; Wartenberg, D.; Rhoads, G. G., Ambient air pollutant concentrations during pregnancy and the risk of fetal growth restriction. Journal of Epidemiology & Community Health 2009, 63, (6), 488-496.
53. Bell, M. L.; Ebisu, K.; Belanger, K., The relationship between air pollution and low birth weight: effects by mother's age, infant sex, co-pollutants, and pre-term births. Environmental research letters : ERL [Web site] 2008, 3, (4), 44003.
54. Savitz, D. A.; Bobb, J. F.; Carr, J. L.; Clougherty, J. E.; Dominici, F.; Elston, B.; Ito, K.; Ross, Z.; Yee, M.; Matte, T. D., Ambient fine particulate matter, nitrogen dioxide, and term birth weight in New York, New York. American journal of epidemiology 2013, 179, (4), 457-466.
55. Merklinger-Gruchala, A.; Kapiszewska, M., Association between PM10 air pollution and birth weight after full-term pregnancy in Krakow city 1995-2009--trimester specificity. Annals of agricultural and environmental medicine : AAEM 2015, 22, (2), 265-70.
56. Chen, G.; Guo, Y.; Abramson, M. J.; Williams, G.; Li, S., Exposure to low concentrations of air pollutants and adverse birth outcomes in Brisbane, Australia, 2003–2013. Science of The Total Environment 2018, 622, 721-726.
57. Dadvand, P.; Parker, J.; Bell, M. L.; Bonzini, M.; Brauer, M.; Darrow, L. A.; Gehring, U.; Glinianaia, S. V.; Gouveia, N.; Ha, E.-h., Maternal exposure to particulate air pollution and term birth weight: a multi-country evaluation of effect and heterogeneity. Environmental health perspectives 2013, 121, (3), 267.
58. Parker, J. D.; Rich, D. Q.; Glinianaia, S. V.; Leem, J. H.; Wartenberg, D.; Bell, M. L.; Bonzini, M.; Brauer, M.; Darrow, L.; Gehring, U., The international collaboration on air pollution and pregnancy outcomes: initial results. Environmental health perspectives 2011, 119, (7), 1023.
59. Kashima, S.; Naruse, H.; Yorifuji, T.; Ohki, S.; Murakoshi, T.; Takao, S.; Tsuda, T.; Doi, H., Residential proximity to heavy traffic and birth weight in Shizuoka, Japan. Environmental research 2011, 111, (3), 377-387.
60. Bruckner, T. A.; Modin, B.; Vågerö, D., Cold ambient temperature in utero and birth outcomes in Uppsala, Sweden, 1915–1929. Annals of epidemiology 2014, 24, (2), 116-121.
61. Anderson, G. B.; Bell, M. L., Heat waves in the United States: mortality risk during heat waves and effect modification by heat wave characteristics in 43 U.S. communities. Environ Health Perspect 2011, 119, (2), 210-8.
62. Leitte, A. M.; Petrescu, C.; Franck, U.; Richter, M.; Suciu, O.; Ionovici, R.; Herbarth, O.; Schlink, U., Respiratory health, effects of ambient air pollution and its modification by air humidity in Drobeta-Turnu Severin, Romania. Science of the Total Environment 2009, 407, (13), 4004-4011.
63. Jo, E.-J.; Lee, W.-S.; Jo, H.-Y.; Kim, C.-H.; Eom, J.-S.; Mok, J.-H.; Kim, M.-H.; Lee, K.; Kim, K.-U.; Lee, M.-K., Effects of particulate matter on respiratory disease and the impact of meteorological factors in Busan, Korea. Respiratory medicine 2017, 124, 79-87.
64. Scovronick, N.; Adair-Rohani, H.; Borgford-Parnell, N., Reducing global health risks through mitigation of short-lived climate pollutants: scoping report for policymakers. Geneva: World Health Organization and Climate and Clean Air Coalition 2015.
65. Kim, S. E.; Honda, Y.; Hashizume, M.; Kan, H.; Lim, Y.-H.; Lee, H.; Kim, C. T.; Yi, S.-M.; Kim, H., Seasonal analysis of the short-term effects of air pollution on daily mortality in Northeast Asia. Science of the Total Environment 2017, 576, 850-857.
66. Sun, X.; Luo, X.; Zhao, C.; Zhang, B.; Tao, J.; Yang, Z.; Ma, W.; Liu, T., The associations between birth weight and exposure to fine particulate matter (PM2. 5) and its chemical constituents during pregnancy: A meta-analysis. Environmental Pollution 2016, 211, 38-47.
67. Schramm, W. F.; Stockbauer, J. W.; Hoffman, H. J., Exercise, employment, other daily activities, and adverse pregnancy outcomes. Am J Epidemiol 1996, 143, (3), 211-8.

68. Wang, Q.; Zhang, H.; Liang, Q.; Knibbs, L. D.; Ren, M.; Li, C.; Bao, J.; Wang, S.; He, Y.; Zhu, L., Effects of prenatal exposure to air pollution on preeclampsia in Shenzhen, China. Environmental Pollution 2018, 237, 18-27.
69. Kim, O.-J.; Ha, E.-H.; Kim, B.-M.; Seo, J.-H.; Park, H.-S.; Jung, W.-J.; Lee, B.-E.; Suh, Y.-J.; Kim, Y.-J.; Lee, J.-T., PM10 and pregnancy outcomes: a hospital-based cohort study of pregnant women in Seoul. Journal of occupational and environmental medicine 2007, 49, (12), 1394-1402

2.6 Modification effects of population expansion, ageing and adaptation on heat-related mortality under climate change scenarios in Guangzhou, China

Tao Liu [1], Zhoupeng Ren [2], Yonghui Zhang [3], Baixiang Feng [1], Hualiang Lin [4], Jianpeng Xiao [1], Weilin Zeng [1], Xing Li [1], Zhihao Li [1], Shannon Rutherford [5], Yanjun Xu [3], Shao Lin [6,7], Philip C. Nasca [6,7], Yaodong Du [8], Jinfeng Wang [2], Cunrui Huang [4], Peng Jia [9,10] and Wenjun Ma [1,*]

[1] Guangdong Provincial Center for Disease Control and Prevention, Guangzhou 511430, China; gztt_2002@163.com (T.L.); fengbaixiang@126.com (B.F.); jpengx@163.com (J.X.); zengwl@gdiph.org.cn (W.Z.); lixing.echo@foxmail.com(X.L.); zhihaoli1990@163.com (Z.L.)

[2] Institute of Geographic Sciences and Natural Resources Research, Chinese Academy of Sciences, Beijing 100101, China; renzp@Lreis.ac.cn (Z.R.); wangjf@Lreis.ac.cn (J.W.)

[3] Guangdong Provincial Center for Disease Control and Prevention, Guangzhou 511430, China; zyh@cdcp.org.cn (Y.Z.); gdxyj05@21cn.com (Y.X.)

[4] School of Public Health, Sun Yat-sen University, Guangzhou 510080, China; hualianglin@gmail.com (H.L.); huangcr@mail.sysu.edu.cn (C.H.)

[5] School of Medicine, Griffith University, Brisbane QLD 4111, Australia; s.rutherford@griffith.edu.au

[6] School of Public Health, University at Albany, State University of New York, One University Pl, Rensselaer, NY 12148, USA; slin@albany.edu (S.L.); pnasca@albany.edu (P.C.N.)

[7] School of Public Health, University at Albany, State University of New York, One University Pl, Rensselaer, NY 12148, USA

[8] Guangdong Provincial Climate Center, Guangzhou 510080, China; yddu@grmc.gov.cn

[9] Faculty of Geo-information Science and Earth Observation (ITC), University of Twente, Enschede 7500, The Netherlands; jiapengff@hotmail.com

[10] International Initiative on Spatial Lifecourse Epidemiology (ISLE), Enschede 7500, The Netherlands

* Correspondence: mawj@gdiph.org.cnTel: +86-20-31051602; Fax: +86-20-31051652

Liu T, Ren Z, Zhang Y, Feng B, Lin H, Xiao J, et al. Modification Effects of Population Expansion, Ageing, and Adaptation on Heat-Related Mortality Risks Under Different Climate Change Scenarios in Guangzhou, China. International Journal of Environmental Research and Public Health 2019;16(3):376.

Abstract:

Background: Although the health effects of future climate change have been examined in previous studies, few have considered additive impacts of population expansion, ageing, and adaptation. We aimed to quantify the future heat-related years of life lost (*YLLs*) under different Representative Concentration Pathways (RCP) scenarios and global-scale General Circulation Models (GCMs), and further to examine relative contributions of population expansion, ageing, and adaptation on these projections.

Methods: We used downscaled and bias-corrected projections of daily temperature from 27 GCMs under RCP2.6, 4.5, and 8.5 scenarios to quantify the potential annual heat-related YLLs in Guangzhou, China in the 2030s, 2060s, and 2090s, compared to those in the 1980s as a baseline. We also explored the modification effects of a range of population expansion, ageing, and adaptation scenarios on the heat-related *YLLs*.

Results: Global warming, particularly under the RCP8.5 scenarios, would lead to a substantial increase in the heat-related *YLLs* in the 2030s, 2060s, and 2090s for the majority of the GCMs. For the total population, the annual heat-related *YLLs* under the RCP8.5 in the 2030s, 2060s, and 2090s were 2.2, 7.0, and 11.4 thousand, respectively. The heat effects would be significantly exacerbated by rapid population expansion and ageing. However, substantial heat-related *YLLs* could be counteracted by the increased adaptation (75% for the total population and 20% for the elderly).

Conclusions: The rapid population expansion and ageing coinciding with climate change may present an important health challenge in China, which, however, could be partially counteracted by the increased adaptation of individuals.

Keywords: climate change; years of life lost; population expansion; ageing; adaptation; population health

Introduction

The Intergovernmental Panel on Climate Change (IPCC) has projected that the increase in global surface temperature will continue in the coming decades [1]. The impacts of high temperature on human health have been reported in many previous studies [2,3]. Hence, the health risk assessment of future climate change could aid in improving the design of public health interventions and policies, preparedness of adaptation strategies, and healthcare planning. Numerous studies have assessed the heat-related mortality risks of future climate change in developed countries, but few were performed in developing countries where health vulnerability to climate change is greater [4,5]. In addition, in the process of assessing health risks, few studies have considered the factors affecting the vulnerability and susceptibility of humans to increasing temperature, such as population ageing and adaptation [6–10].

Ageing is an important determinant of human vulnerability to increasing temperature, as the elderly are more at risk from extreme heat events [11,12]. In addition, people can also acclimatize to climate change through physiological and technical adaptations [13–15]. Therefore, it is vital to integrate these factors into the health risk assessment of future climate change, which can broaden our understanding of the emerging health risks caused by climate change.

In this study, we projected the future heat-related years of life lost (*YLLs*) in Guangzhou, China, for the 2030s, 2060s, and 2090s under three Representative Concentration Pathways (RCP) scenarios (RCP2.6, 4.5, and 8.5) and 27 global-scale General Circulation Models (GCMs). The relative contributions of population expansion, ageing, and adaptation to these heat-related *YLLs* were also examined.

Materials and Methods

Study Settings

Guangzhou city is the third largest metropolis and the capital of Guangdong Province in South China (Figure S1). In 2010 it had a population of 12.7 million, of which 6.62% were 65 years and over [16]. The ambient temperature in Guangzhou increased at a rate of 0.13 °C per decade during 1951–2004, which was higher than the national average rate (0.04 °C per decade). In particular, the ambient temperature increased more rapidly after the 1980s, which makes it one of the cities with the most rapid increase in temperature in China [17]. In addition, it is expected that the ambient temperature in Guangzhou will continue to increase in future decades [1].

Data Collection and Preparation

Daily non-accidental mortality data in Guangzhou during 2010–2015 were obtained from the Guangdong Provincial Center for Disease Control and Prevention (GDCDC). Non-accidental deaths were categorized using A00-R99 codes from the International Classification of Diseases 10th Revision (ICD-10). *YLLs* were calculated by matching each death by age and sex to the life table of China for the year 2010

[18]. Total daily *YLLs* were calculated by summing the *YLLs* for all deaths on the same day. We also estimated the daily *YLLs* for males, females, and people aged <65 and ≥65 years, respectively.

Historical daily meteorological data, including daily mean temperature (*TM*), relative humidity (*RH*) and wind speed (*WS*), for the 1980s and 2010–2015 in Guangzhou, were collected from the Guangdong Provincial Meteorological Bureau. The 1980s were chosen as our modelling baseline because this decade is at the centre of the conventional climatological baseline period from 1971 to 2000, which was also employed in several previous studies [19,20]. The *YLLs* estimated during the baseline period were subtracted from heat-related *YLLs* for future periods. Meteorological data during the 2010–2015 were used to assess the exposure-response relationship between high temperature and YLLs in Guangzhou, because these data are the most updated and hence can be matched to the most recent census data in 2010.

Future daily temperature data projected using 27 GCMs under three RCP scenarios were collected from Coupled Model Inter-comparison Project 5 (CMIP5) (Table S1) [1,21]. A single ensemble was used for each GCM model. We chose RCP2.6, RCP4.5, and RCP8.5 scenarios to represent the low, middle, and high greenhouse gas (GHG) emissions, respectively. Because GCMs often provide biased simulated temperature which is usually at coarse spatial resolution [22], we employed three bias-correction models (*unbiasing*, *qqmap*, and *isi-mip*) to downscale the projected temperature data to a finer spatial resolution of 0.5 °C × 0.5 °C [23], in which the daily TM data of 680 meteorological stations during 1960–1999 in China [24] was used as a training dataset. We finally selected the results derived from *isi-mip* as input for projection as it outperformed the other two methods (Figure S2). The output corresponding to the geographical location of Guangzhou was used.

Daily air pollutant data, including NO_2 (nitrogen dioxide), SO_2 (sulfur dioxide), and PM_{10} (particulate matter with an aerodynamic diameter of 10 μm or less) during 2010–2015 were obtained from Guangzhou Environmental Monitoring Center.

Population expansion was indicated by the total population size. The population information (total population size and its sex and age structures) in Guangzhou in the 2030s, 2060s and 2090s was projected using the framework employed by the United Nations Population Estimates and Projections [25,26]. Based on this framework, we integrated historical sex- and age-specific mortality rates, total fertility rate (*TFR*), population counts (population size and migration), life expectancy at birth and sex ratio from 5-year periods during 1950–2015 in Guangzhou. The historical (1950–2015) and projected *TFRs* (2020–2100), and historical period sex- and age-specific mortality rates (1950–2015) were obtained from the United Nations provided at the Chinese national level data, as the Guangzhou city-specific data were not available. However, available mortality data for several years (i.e., 2010) indicated that the mortality rates for the total population, males, and females in Guangzhou were similar to the national levels [27]. The historical population size and sex ratio data were collected from the Guangzhou Statistical Yearbook [28]. Historical life expectancy at birth was obtained from several previous studies [29–31]. Based on these historical data, we first generated the probabilistic projections of sex-specific life expectancies at birth for 2020–2100 using a Bayes hierarchical model [32]. A sample of 10,000 trajectories of future life expectancy was estimated to show their probability distribution. Then the period probabilistic population projections for 2020–2100 were estimated using the standard cohort-component model [33]. This method provides a sample of 10,000 values of any future population quality to approximate its predictive distribution. To consider the uncertainty of projection, we employed the median and 90% interval of projection trajectories to respectively represent the medium, low and high scenarios of population index increases in the future: total population size, sex-and age-specific population size, and proportion of the elderly population (≥65 years) (Please refer to Figure S3 and Table S2 for details).

Adaptation was defined by the IPCC as "the process of adjustment to actual or expected climate and its effects" [34]. The main types of climate change adaptation include physiological adaptation (or acclimatization), behavioural (e.g., air conditioning), infrastructure (e.g., healthcare systems), and technological adaptation (e.g., heat warning systems) [15]. In this study, we employed three adaptation scenarios in this study to capture their effects on heat-related health effects. In the first scenario (S1), we assumed that people's adaptation would increase by 8.92% per decade [35], which was estimated by Yang's study conducted in Shanghai that has the similar socioeconomic characteristics with Guangzhou. In Yang's study, they assessed the long-term variation in the association between ambient temperature and daily cardiovascular mortality in Shanghai from 1981 to 2012. Their findings showed that the extremely hot effects (99th percentile of mean temperature) decreased by 8.92% per decade. This is a unique study that has assessed the long-term variation of heat effects in China. However, the 30-year study duration might not capture the long-term variation of people's adaptation. In addition, Yang et al. assessed only heat effects on cardiovascular mortality. Therefore, we used another adaptation scenario (S2) that was from Petkova et al.'s study conducted in New York City. This study quantitatively assessed the effects of people's adaptation on daily temperature impacts over a period spanning more than a century [36]. They observed that a decrease in heat effects of 4.6% per decade could be attributed to people's adaptation. In addition, people's adaptation to high temperature could also be measured by the change of minimum mortality temperature (*MMT*) that is the temperature with the lowest mortality risk. The increase of *MMT* over time suggests improved adaptation to heat effects [37]. In a recent study, Todd and Valleron assessed the temperature-mortality relationship in France from 1968 to 2009, and observed that the *MMT* increased by about 0.2 °C/decade [38]. In this study, we also employed the change of *MMT* to assess people's adaptation (S3), and assumed (consistent with Todd and Valleron, 2015) that the *MMT* would also increase by 0.2 °C per decade in Guangzhou.

Heat Effects Estimation

We first employed a distributed lag non-linear model (DLNM) [39] to estimate the non-linear and lag effects of heat effects on *YLLs* for all deaths during 2010–2015. The model can be written as:

$$YLL_t = \alpha + \beta T_{t,l}(\mathrm{TM}) + ns(\mathrm{RH}, df) + ns(\mathrm{WS}, df) + ns(\mathrm{time}_t, df) + ns(\mathrm{SO_2}, df) + ns(\mathrm{NO_2}, df) + ns(\mathrm{PM_{10}}, df) + \eta \mathrm{DOW} \quad (1)$$

where t denotes the day of observation; YLL_t denotes the total *YLLs* on day t; α denotes the intercept indicating the baseline risk. $T_{t,l}$ is a matrix obtained by applying the DLNM to *TM*; β denotes the vector of coefficients for $T_{t,l}$, and l denotes the number of lag days. We employed a B-spline function (*bs*) and a natural cubic spline function (*ns*) to estimate the non-linear and lagged effect of *TM*, respectively. We fitted a lag structure of up to 1 day (lag 0–1) according to our preliminary analysis which showed that the heat effects mainly appeared during the first two days (Figure S4). The family function for DLNM was Gaussian. Degrees of freedom (*df*) for the lag structure were chosen based on Akaike information criterion (AIC) [40]. It was found that 3*df*s for non-linear effects of *TM* produced the best model fit. The *df*s for RH, WS, SO_2, NO_2, and PM_{10} were all set to 3, consistent with some previous studies [41,42]. 5*df*s per year was used to control for secular trend indicated by *time* that equals 1, 2, 3, . . . 2191 (day of the study period 2010–2015). DOW is a dummy variable representing day of the week, and η is a vector of coefficients.

Based on equation (1), a healthy temperature range (*TM*) of 12.6–21.0 °C, within which the heat effects were not statistically significant, was identified. A temperature of 21.0 °C was defined as the threshold temperature, and all the cumulative effects (*YLLs*) of temperature above 21.0 °C along lag 0–1 day were defined as heat effects. Similarly, we defined the heat effect threshold temperature in males (24.3 °C), females (21.5 °C), and people <65 (28.5 °C) and ≥65 years (elderly) (18.6 °C).

Projection of Future Heat Effects

The heat-related *YLLs* under each RCP scenario (RCP2.6, 4.5 and 8.5) and GCM were estimated using modelled daily *TM* in the 1980s, 2030s, 2060s, and 2090s, respectively. The calculation process is described as:

$$YLL' = \sum_{t=21.0}^{n} YLL_t \times N_{TM} \quad (2)$$

where *YLL′* denotes the total heat-related *YLLs*. YLL_t denotes the attributable *YLLs* of $TM \geq 21.0$ °C which was obtained by equation (1); n is the maximum of daily TMs during each study period. N_{TM} is the average annual number of days with TM ≥ 21.0 °C. Then, we estimated the differences in annual heat-related YLLs between the future and 1980s as a baseline under each RCP scenario and each GCM. Here, we assumed that the population size and their adaptation in the 2030s, 2060s and 2090s would remain constant at the 2010 level.

To test the independent impacts of population expansion on the future heat-related *YLLs*, we estimated the population expansion adjusted heat-related *YLLs*:

$$YLL'_p = YLL' \times U_{20X0}/U_{2010} \quad (3)$$

where YLL'_p denotes the annual heat-related *YLLs* after taking into account the population expansion level. U_{20X0} denotes the projected population expansion in Guangzhou in the future (2030s, 2060s and 2090s), and U_{2010} denotes the population size in Guangzhou in 2010. Similarly, we calculated the population expansion adjusted annual heat-related *YLLs* (YLL'_{ep}) in the elderly.

While assessing the impacts of the degree of ageing (percentage of elderly ≥65 years in the total population) on the future heat-related YLLs, the impacts of total population size could not be ignored, because more people will enter this age range along with the increase in population size. Therefore, we used equation (4) to estimate the heat-related YLLs for the elderly in every one million total populations, and then explored the relationship between the degree of ageing and the heat-related *YLLs* for the elderly, which could be used to adjust for the bias of total population sizes:

$$YLL'_{p/m} = YLL'_{ep}/P_{20X0} \quad (4)$$

where $YLL'_{p/m}$ denotes the annual heat-related *YLLs* of the elderly for every one million total populations under different scenarios of population increase. YLL'_{ep} denotes the annual heat-related *YLLs* for the elderly in the future after taking into account the population expansion. P_{20X0} denotes the total population size (million) in Guangzhou in the future.

We also assessed the impacts of adaptation on the heat effects in the future. We considered three adaptation scenarios. In adaptation S1, people's adaptation was assumed to increase by 8.92% per decade [35]:

$$YLL'_a = YLL' \times (1 - 0.0892)^Z \quad (5)$$

where YLL'_a denotes the annual heated-related *YLLs* in the future after deducting the heat effects offset by people's increasing adaptation. 0.0892 (8.92%) is the decrease in rate of heat effects per decade. *Z* denotes the difference in number of decades between future study projection years (2030s, 2060s, and 2090s) and 2010. Similarly, we estimated the adjusted heated-related *YLLs* in the future if people's adaptation increased by 4.60% per decade [36]. In adaptation S3, we assumed that the MMT in the nonlinear relationship between TM and YLLs would increase by 0.2 °C/decade [38]. For example, the (*TM* + 0.4) in the 2030s would lead to the same heat-related health effects with *TM* in the 2010s. Equation (5) is used to illustrate the process in the total population as an example:

$$YLL'_{a3} = \sum_{t=21.0}^{n} YLL_t \times N_{TM-Z\times 0.2} \quad (6)$$

where YLL'_{a3} denotes the annual heated-related *YLLs* in the future. *TM* denotes the daily mean temperature in the future. $N_{TM-Z\times 0.2}$ denotes the annual number of days with ($TM-Z \times 0.22$) ≥ 21.0°C. *Z* denotes the difference in number of decades between future study projection years (2030s, 2060s and 2090s) and 2010. YLL_t is the attributable *YLLs* on day t with a ($TM-Z \times 0.2$) ≥ 21.0°C as compared with the *YLLs* in days with the healthy temperature. n is the maximum daily temperature ($TM - Z \times 0.2$). For example, the attributable *YLLs* on the day with a TM of 25.2 °C in the 2030s was defined as the average *YLLs* on the day with a TM of 25.0 (25.2–0.4) °C in the 2010s in Guangzhou.

Finally, we estimated the impacts of both adaptation and population expansion on the heat effects:

$$YLL'_{pa} = YLL' \times \frac{U_{20X0}}{U_{2010}} \times (1 - 0.0892)^Z \quad (7)$$

where YLL'_{pa} denotes the annual heated-related *YLLs* in the future after taking into account both population expansion and adaptation; U_{20X0} and U_{2010} denote the population expansion levels in the future and 2010s respectively. Similarly, we also estimated the YLL'_{pa} under the other two scenarios of adaptation.

All the above calculation processes were conducted for males, females, and people aged <65 and ≥65 years. We used R software (version 3.4.0; R Development Core Team 2012, http://www.R-project.org/, Vienna, Austria) to fit all models.

Results

General Characteristics

In Guangzhou during 2010–2015, the annual *TM* was 21.9 °C and the average total daily *YLLs* was 2408.7 (Table 1). The 27GCM outputs indicate that temperature will increase more rapidly under the RCP8.5 and RCP4.5 scenarios than the RCP2.6 scenario, and the average increase in temperature was 0.023, 0.125, and 0.320 °C per decade for the three scenarios, respectively (Figure 1 and Table S3). According to the population projections, the total population in Guangzhou will peak during the 2030s and then decrease after 2040 under the low and medium scenarios, but it will keep increasing in the high scenario (Figure S3). We observed a typical U-shaped relationship between *TM* and *YLLs* along lag 0−1 days from 2010 to 2015 (Figure 2 and Figure S5).

Independent Effects of Temperature Increase on Heat-Related Ylls in the 2030s, 2060s, and 2090s

Without integrating urbanization and adaptation, we observed a predominant increasing trend in the *YLLs* for the three future periods under all RCP scenarios and the majority of 27 GCMs, although there were large variations in *YLLs* among GCMs. The increments of *YLLs* were more rapid under the RCP4.5 and RCP8.5 scenarios compared with the RCP2.6 scenario. For the total population, the annual heat-related YLLs in the 2030s, 2060s, and 2090s were 1.6, 2.4, and 2.5 thousand, respectively, under RCP2.6, and the corresponding figures were 2.2, 7.0, and 11.4 thousand, respectively, under RCP8.5 compared with the baseline range (Figure 3 and Figure S6).

Table 1. Mean, range, and specific percentiles for studied variables in Guangzhou during 2010–2015.

Variables	Mean	Min	25th	75th	Max
Total *YLLs* per day	2408.7	982.7	2035.2	2716.5	4171.6
Gender					
Males	1455.1	522.5	1208.8	1666.4	2652.7
Females	953.5	360.2	785.2	1095.1	1982.9
Age groups					
<65 years	1486.6	588.8	1206.9	1712.0	2987.0
≥65 years	922.1	355.0	766.4	1066.1	1731.8
Mean temperature (°C)	21.9	4.8	17.3	27.2	32.2
Wind speed (m/s)	2.3	0.3	1.5	2.7	9.5
Relative humidity (%)	77.6	30.0	71.0	85.0	100.0
Mean temperature (°C) during 1980s	22.0	3.9	16.8	27.3	32.7
SO_2 (μg/m^3)	22.2	2.0	13.1	27.7	106.5
NO_2 (μg/m^3)	44.9	9.8	29.5	54.5	345.8
PM_{10} (μg/m^3)	68.9	9.6	44.1	87.0	419.8

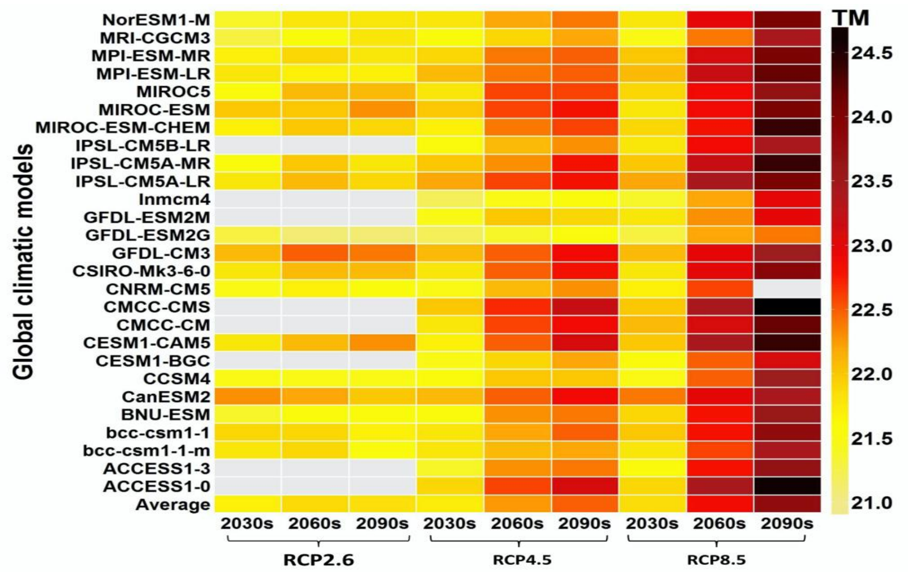


Figure 1. Annual temperature in the 2030s, 2060s, and 2090s under different climatic models and RCP scenarios. Grey grids mean that the data were not available.

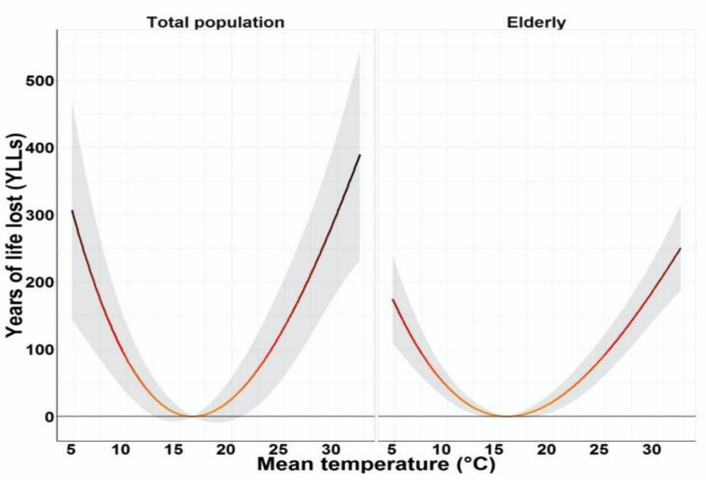


Figure 2. Relationships between daily mean temperature and *YLLs* in the total population and the elderly. All the effects of temperature on *YLLs* were adjusted for secular trend, wind speed, day of week, relative humidity, SO_2, NO_2, and PM_{10}.

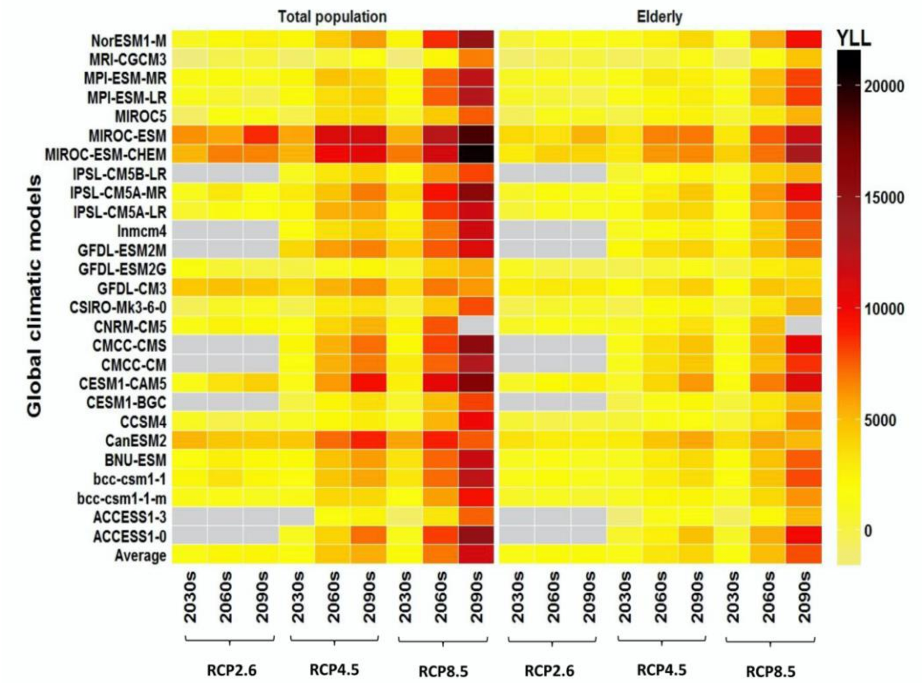


Figure 3. Annual heat-related *YLLs* in the total population and the elderly under different climatic scenarios. Note: The heat-related *YLLs* in the future have been subtracted by the heat-related *YLLs* in the 1980s. We assumed that the population size and their adaptation in the 21st century would remain constant at the 2010 level. Grey grids mean that the data were not available.

Modification of Population Expansion and Adaptation on Heat-Related YLLs in the 2030s, 2060s, and 2090s

During the 2030s, when the population will reach its peak, compared with the scenario of constant population size at the 2010 level, we observed a more rapid increase in heat-related YLLs from low, medium to high population expansion under all climate change scenarios if the adaptation was constant. Each 10% increase in population expansion level was associated with an average of 4.23, 4.23, and 4.29 thousand more *YLLs* under the RCP2.6, RCP4.5, and RCP8.5 scenarios, respectively, in the 2030s (Table S4). For the 2060s, we observed a similar trend in heat-related *YLLs* as the 2030s from low, medium to high expansion scenarios, but the *YLLs* under the low expansion scenario were lower than the constant expansion scenario. In terms of the 2090s, *YLLs* under low as well as medium expansion scenarios are smaller than the constant expansion scenario, but the changing trend in *YLLs* from low, medium to high expansion is consistent with the 2030s and 2060s. One of the major reasons for the *YLL* decrease is a decrease in population size under the low and medium scenarios.

After considering adaptation, we found that heat-related *YLLs* would be largely counteracted under adaptation S1 (8.92% decrease per decade) and S3 (0.2 °C increase in MMT per decade) scenarios, but less modified under adaptation S2 scenario (4.60% decrease per decade) for the total population. For example, 78.0%, 77.9%, and 74.4% of heat-related *YLLs* under high population expansion scenarios in the 2030s could be offset by adaptation (S1) under the RCP2.6, RCP4.5, and RCP8.5 scenarios, respectively, and the figures declined to 14.7%, 14.8%, and 14.1%, respectively, under the adaptation S2 scenario. Furthermore, the heat-related YLLs could also be subsequently offset by adaptation in the 2060s and 2090s (Figure 4 and Table S4).

We found future changing patterns of heat-related *YLLs* in the total population to be similar to patterns in males, females and the elderly population. In particular, we observed more rapid increases of heat-related *YLLs* in the elderly due to the rapid ageing of the population. Detailed information is shown in Figures S7–S10.

Modification of Population Ageing and Adaptation on Heat-Related YLLs in the 2030s, 2060s, and 2090s

Figure 5 shows that the increased ageing (as measured by percentage of the elderly in the total population) will result in a significant increase in heat-related *YLLs* when adaptation is considered to be constant since 2010. Each 1% increase in the degree of ageing will lead to an average of 428.0 more *YLLs* in one million total population in the 2030s. Moreover, the ageing induced heat-related *YLLs* will consecutively increase as time progresses, and reach a peak in the 2090s. The heat-related *YLLs* in the future could be largely counteracted under the S1 and S3 adaptation scenarios, particularly in the 2060s and 2090s when people's adaptation consecutively increases. The average *YLLs* for each 1% increase in ageing decreased from 428.0 to 368.5. The offset effects of the S2 adaptation were less than S1 and S3 (Figure 5).

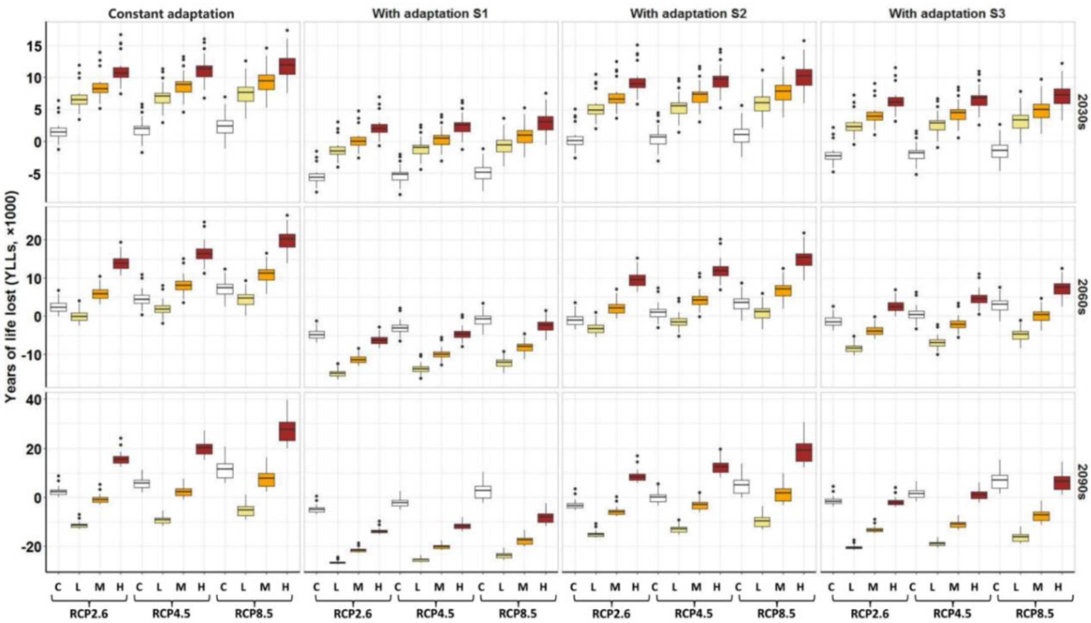


Figure 4. Impacts of population expansion and adaptation on the annual heat-related *YLLs* in the future. Constant adaptation: People's adaptation to high temperature will remain constant at the 2010 level. Adaptation S1: People's adaptation to high temperature will increase by 8.92% per decade. Adaptation S2: People's adaptation to high temperature will increase by 4.60% per decade. Adaptation S3: People's adaptation to high temperature will increase by 0.2 °C per decade. C: The population size will remain constant at the 2010 level. L: Low population expansion scenario. M: Medium population expansion scenario. H: High population expansion scenario. The three rows of panel show the effects of population expansion and adaptation on the heat-related *YLLs* in 2030s, 2060s, and 2090s, respectively. The heat-related *YLLs* in the future have been subtracted by the heat-related *YLLs* in the 1980s.

Discussion

Climate change is not only a significant environmental issue, but also a serious public health challenge that may continue to grow as the planetary temperature increases. In this study, we found that heat-related *YLLs* in Guangzhou, China would dramatically increase under all climate change scenarios and most GCMs as the 21st century progresses. This finding was consistent with those of some previous studies. For example, in comparison with the 1980s, Li et al. identified that cardiovascular mortality in Beijing under the RCP8.5 scenario would increase by 16.6%, 73.8%, and 134.0% in the 2020s, 2050s, and 2080s, respectively [6]. These findings highlighted the potential public health benefits that could result from the scenario of lower GHG emission and the critical importance of adequately adapting to climate change to protect vulnerable populations if we cannot reverse the trend of global warming in the near future.

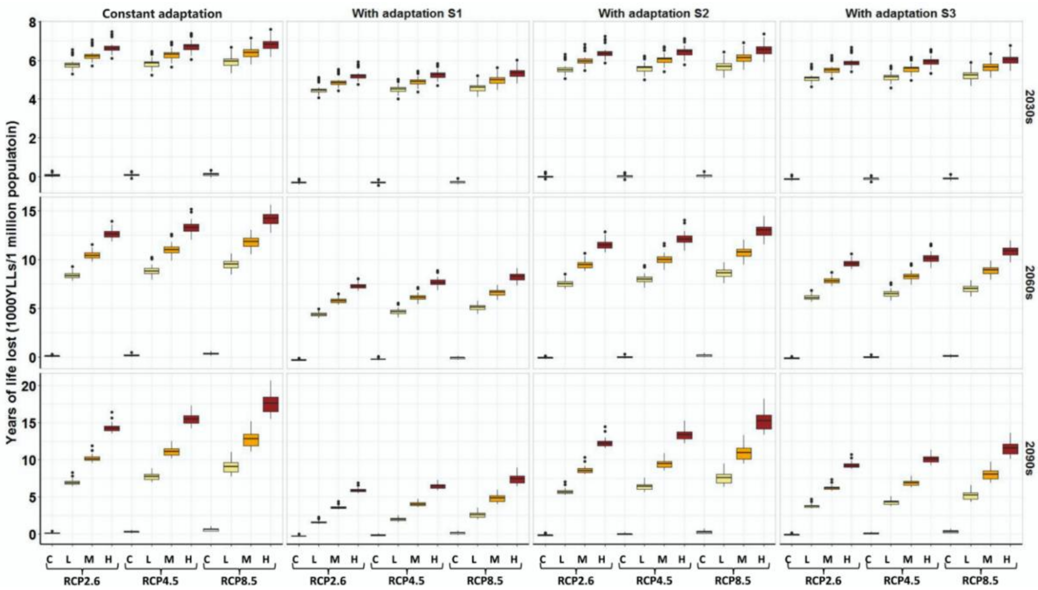


Figure 5. Impacts of ageing and adaptation on the annual heat-related *YLLs* in the future. Constant adaptation: People's adaptation to high temperature will remain constant at the 2010 level. Adaptation S1: People's adaptation to high temperature will increase by 8.92% per decade. Adaptation S2: People's adaptation to high temperature will increase by 4.60% per decade. Adaptation S3: People's adaptation to high temperature will increase by 0.1 °C per decade. C: The population size will remain constant at the 2010 level. L: Low population expansion scenario. M: Medium population expansion scenario. H: High population expansion scenario. The three rows of panel show the effects of ageing and adaptation on the heat-related *YLLs* in 2030s, 2060s, and 2090s, respectively. The heat-related *YLLs* in the future have been subtracted by the heat-related *YLLs* in the 1980s.

We further found that rapid population expansion would significantly aggravate adverse heat-related effects under all climate change scenarios. It has been demonstrated that rapid population expansion, especially in urban areas, could lead to land use/cover change, pollution, overcrowding, changes in physical activity patterns, and inadequate service capacity for sanitation. All of them could elevate the human risk for climate change [8]. Hence, it is possible that urban areas where the population has been growing fastest are also those that are least equipped to deal with the threat of climate change.

We used three population expansion scenarios (i.e., low, medium, and high) to assess uncertainties in the influences of future population expansion on heat effects, and observed that heat-related *YLLs* would decrease under the low and medium expansion scenarios in the 2060s and 2090s. One major reason for the reduction in *YLLs* is a decrease in population size under the low and medium scenarios, where the population would consecutively decline after 2040. However, the population expansion process in Guangzhou would probably follow the high scenario because of the universal two-child policy issued by the Chinese government in October 2015, which aimed to attenuate negative effects of the one-child policy, such as accelerating population ageing, the skewed sex ratio, and the decline of working-age populations [43]. It has been projected that the total fertility rate in urban areas would significantly increase in the next several decades [44], which will lead to a rapid increase in population size in megacities such as Guangzhou. These results suggest that the rapid population expansion will lead to unprecedented challenges in dealing with health threats of future climate change, and the heat-related health risks would be greatly underestimated if population expansion was not integrated into assessment models. Policy makers need to adequately consider actions to enhance sustainable development and urban resilience to the health impacts of climate change, such as through the reduction in GHG emissions (mitigation) and the increase in adaptation [45].

It has been observed that the elderly were more vulnerable to climate change [11,12] Ageing can decrease an individual's tolerance to heat. The elderly also often suffer from comorbidity, social isolation, physical and cognitive impairment, and the need to take multiple medications, which may further increase their vulnerability to extreme heat [46]. Here, we found that the heat-related *YLLs* in the elderly were projected to increase more rapidly than other age groups. For example, we estimated that every 1% increase in the percentage of the elderly per one million population would be associated with an increase in around 420 heat-related YLLs in the 2030s; this figure would increase further in the 2060s and 2090s. A recent study conducted in Beijing observed similar results [6]. In the coming decades, China will go through a rapidly ageing stage due to the baby boom several decades ago. We estimated that the number of the elderly under the medium scenario in Guangzhou would increase from 0.84 million (6.62%) in 2010 to 3.5 (23.7%), 4.9 (35.7%), and 4.2 million (36.0%) in the 2030s, 2060s, and 2090s, respectively. Although the implementation of the universal two-child policy may partially alleviate the degree of ageing in the future, the absolute number of the elderly would be very large in the future [43]. Hence, the protection for the elderly should be prioritized in dealing with the adverse effects of global warming. Strategies that have enhanced the care of the elderly and improve their ability to cope with climate change, such as regular monitoring of their health conditions, encouraging suitable clothing, providing cool environments, appropriate diets, and adequate intake of fluids, need to be implemented particularly at the community level as most elderly people live with their families in the community.

Our results further revealed that adaptation would significantly offset the future heat effects, which was consistent with previous studies' findings. For instance, Jenkins et al. observed that increasing the temperature threshold for … by 1 °C could result in declines in annual heat-related mortality ranging from 32% to 42% across the scenarios in London in the 2050s [47]. These findings repeatedly reminded us of the vital importance of adaptation in response to climate change, and that strategies such as heat plans [48] and other specific measures should be implemented to improve people's adaptation. For example, properly designed infrastructure can provide physical protection; well-designed communications and early warning systems can help people to respond and cope with heat waves; and appropriate urban planning including land-use changes, building regulations, external shading, green space increase, and GHG mitigation can reduce heat exposure and hence help to reduce heat impacts.

Projecting future adaptation to heat is an important challenge in assessing the heat-related mortality of climate change. In previous studies, methods used to account for adaptation included analogue cities, analogue summers, and assuming adaptation to heat for a pre-determined number of degree Celsius [49], but very few used the past declines invulnerability to temperature [6,7]. In addition, the adaptation may vary along with the process of climate change. For example, more intensive warming process may enhance people's adaptive capacity. Therefore, we employed three adaptation scenarios in this study to assess the uncertainties of offset effects of adaptation on heat-related *YLL* estimations. Of the three scenarios, two were assessed based on the past declines invulnerability to temperature, and one was based on a pre-determined change in temperature units of degrees Celsius. We observed that the adaptation S1 scenario would bring larger offset effects than the other two scenarios. The adaptation S1 scenario might be the most accurate trajectory for people in Guangzhou in the future. We believe that these estimates of heat effects derived from a broad range of scenarios provide uncertainty information for policymakers concerned with adaptation planning for climate change and health.

Limitations and Uncertainties

Some other limitations and uncertainties should be acknowledged in this study. The first source comes from the projection of population expansion. Although we have thought over the uncertainty and employed a probabilistic model in our projection, we ignored the variation of vulnerability to temperature between immigrants from other places and the residents in Guangzhou because we could not project the age and gender structures of these immigrants. However, rural residents in China are more vulnerable to high temperature than urban residents, due to such factors as greater age, lower education, lower incomes, and less access to high-quality medical care. Second, we did not adjust for other air pollutants such as O_3, CO, and $PM_{2.5}$ in the DLNM because of lack of data, which may have led to potentially biased exposure-responses between temperature and *YLLs*. However, previous studies have demonstrated that the effects of air pollutants would be smaller than temperature, and did not significantly alter the effect sizes of temperatures [50].

Furthermore, some air pollutants such as O_3 might be on the causal path between temperature and health, which can also complicate interpretation of adjusted models. Thirdly, we observed weaker associations of TM with YLLs in males and younger people. For example, the YLLs were significantly increased for people <65 years when TMs were larger than 28.5 °C, which may lead to underestimation of the heat effects. Another source of uncertainty is that we did not address the cold-related YLLs, although the reduction of cold-related mortality due to the warming climate change may partially offset the heat-related YLLs. Uncertainties may also come from some other sources, such as possible changes in humidity, air quality affected by climatic factors, health conditions of people, profile of the heatwave, intraurban variation of temperatures and risks, and changing of land-cover, building environments, quality and type of building stock, and population density. These uncertainties are expected to be included in future studies, and thus moving towards a more comprehensive risk-type framework that explicitly represents uncertainty in the assessment.

Conclusions

Our study comprehensively quantified the heat-related *YLLs* of future warming climate under the RCP scenarios on a local scale in China, observing an escalation of heat-related *YLLs* under all scenarios in the 21st century. The heat effects may increase dramatically with continued rapid population expansion processes and population ageing in the future. However, the adaptation increase would partially offset the heat-health effects. Therefore, it is necessary to design and implement more effective response strategies and measures in the future to reduce the heat risk in highly populated urban areas, by reducing heat exposure in all populations, improving their adaptation, and targeting most efforts on the elderly.

References

1. Stocker, T.F.; Qin, D.; Plattner, G.-K.; Tignor, M.; Allen, S.K.; Boschung, J.; Nauels, A.; Xia, Y.; Bex, V.; Midgley, P.M. *IPCC, 2013: Climate Change 2013: The Physical Science Basis*; Contribution of Working Group I to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change; Cambridge University Press: Cambridge, UK; New York, NY, USA, 2013.
2. Guo, Y.; Gasparrini, A.; Armstrong, B.; Li, S.; Tawatsupa, B.; Tobias, A.; Lavigne, E.; de Sousa Zanotti Stagliorio Coelho, M.; Leone, M.; Pan, X.; et al. Global Variation in the Effects of Ambient Temperature on Mortality: A Systematic Evaluation. *Epidemiology* **2014**, *25*, 781–789.
3. Phung, D.; Thai, P.K.; Guo, Y.; Morawska, L.; Rutherford, S.; Chu, C. Ambient temperature and risk of cardiovascular hospitalization: An updated systematic review and meta-analysis. *Sci. Total Environ.* **2016**, *550*, 1084–1102.
4. Huang, C.; Barnett, A.G.; Wang, X.; Vaneckova, P.; FitzGerald, G.; Tong, S. Projecting future heat-related mortality under climate change scenarios: A systematic review. *Environ. Health Perspect.* **2011**, *119*, 1681–1690.
5. Gosling, S.N.; Lowe, J.A.; McGregor, G.R.; Pelling, M.; Malamud, B.D. Associations between elevated atmospheric temperature and human mortality: A critical review of the literature. *Clim. Chang.* **2009**, *92*, 299–341.
6. Li, T.; Horton, R.M.; Bader, D.A.; Zhou, M.; Liang, X.; Ban, J.; Sun, Q.; Kinney, P.L. Aging will amplify the heat-related mortality risk under a changing climate: Projection for the elderly in Beijing, China. *Sci. Rep.* **2016**, *6*, 28161.
7. Petkova, E.P.; Vink, J.K.; Horton, R.M.; Gasparrini, A.; Bader, D.A.; Francis, J.D.; Kinney, P.L. Towards more comprehensive projections of urban heat-related mortality: Estimates for New York City under multiple population, adaptation, and climate scenarios. *Environ. Health Perspect.* **2016**, *125*, 47–55.
8. Li, X.; Song, J.; Lin, T.; Dixon, J.; Zhang, G.; Ye, H. Urbanization and health in China, thinking at the national, local and individual levels. *Environ. Health* **2016**, *15* (Suppl. 1), 32.
9. Lee, J.Y.; Kim, H. Projection of future temperature-related mortality due to climate and demographic changes. *Environ. Int.* **2016**, *94*, 489–494.
10. Zhang, B.; Li, G.; Ma, Y.; Pan, X. Projection of temperature-related mortality due to cardiovascular disease in beijing under different climate change, population, and adaptation scenarios. *Environ. Res.* **2018**, *162*, 152–159.
11. Wu, W.; Xiao, Y.; Li, G.; Zeng, W.; Lin, H.; Rutherford, S.; Xu, Y.; Luo, Y.; Xu, X.; Chu, C.; et al. Temperature-mortality relationship in four subtropical Chinese cities: A time-series study using a distributed lag non-linear model. *Sci. Total Environ.* **2013**, *449*, 355–362.
12. Zeng, W.; Lao, X.; Shannon, R.; Xu, Y.; Xu, X.; Lin, H.; Liu, T.; Luo, Y.; Xiao, J.; Hu, M.; et al. The effect of heat waves on mortality and effect modifiers in four communities of Guangdong Province, China. *Sci. Total Environ.* **2014**, *482–483*, 214–221.
13. Hajat, S.; O'Connor, M.; Kosatsky, T. Health effects of hot weather: From awareness of risk factors to effective health protection. *Lancet* **2010**, *375*, 856–863.
14. Vardoulakis, S.; Dear, K.; Hajat, S.; Heaviside, C.; Eggen, B. Comparative assessment of the effects of climate change on heat- and cold-related mortality in the United Kingdom and Australia. *Environ. Health Perspect.* **2014**, *122*, 1285–1292.
15. Hondula, D.M.; Balling, R.C.; Vanos, J.K.; Georgescu, M. Rising Temperatures, Human Health, and the Role of Adaptation. *Curr. Clim. Chang. Rep.* **2015**, *1*, 144–154.
16. Guangzhou Statistics Department. The Gender and Age Structure of Population in Guangzhou: Data from the Sixth National Census 2013. Available online: http://www.gzstats.gov.cn/pchb/rkpc6/t1-07.htm (accessed on 19 February 2017).

17. Lin, P. Analysis on the Climate Characteristic and Climatic Change in Guangzhou City in Last 50 Years. *J. Liaocheng. Univ.* **2007**, *3*, 81–84.
18. World Health Organization. Global Health Observatory Data Repository: Life Tables by Country, China. Available online: http://apps.who.int/gho/data/?theme=main&vid=60340 (accessed on 15 September 2013).
19. Li, T.; Ban, J.; Horton, R.M.; Bader, D.A.; Huang, G.; Sun, Q.; Kinney, P.L. Heat-related mortality projections for cardiovascular and respiratory disease under the changing climate in Beijing, China. *Sci. Rep.* **2015**, *5*, 11441.
20. Li, T.; Horton, R.M.; Kinney, P.L. Projections of seasonal patterns in temperature-related deaths for Manhattan, New York. *Nat. Clim. Chang.* **2013**, *3*, 717–721.
21. Bureau of Reclamation. *Downscaled CMIP3 and CMIP5 Climate and Hydrology Projections: Release of Downscaled CMIP5 Climate Projections, Comparison with Preceding Information, and Summary of User Needs*; U.S. Department of the Interior, Bureau of Reclamation, Technical Services Center: Denver, CO, USA, 2013. Available online: http://apps.who.int/gho/data/?theme=main&vid=60340 (accessed on 3 January 2019).
22. Schmidli, J.; Frei, C.; Vidale, P.L. Downscaling from GCM precipitation: A benchmark for dynamical and statistical downscaling methods. *Int. J. Climatol.* **2006**, *26*, 679–689.
23. Marsh, C.; Barwell, L.; Gavish, Y.; Kunin, W. Downscale: An R package for downscaling species occupancy from coarse-grain data to predict occupancy at fine-grain sizes. *J. Stat. Softw.* **2018**, *86*, 1–20.
24. Chinese Surface Stations for Global Exchange (V3.0). Available online: http://data.cma.cn/ (accessed on 1 August 2016)
25. United Nations, Department of Economic and Social Affairs, Population Division. *World Population Prospects: The 2015 Revision, Methodology of the United Nations Population Estimates and Projections*; Working Paper No. ESA/P/WP.242; United Nations: New York, NY, USA, 2015.
26. Raftery, A.E.; Li, N.; Ševčíková, H.; Gerland, P.; Heilig, G.K. Bayesian probabilistic population projections for all countries. *Proc. Natl. Acad. Sci. USA* **2012**, *109*, 13915–13921.
27. Song, S.; Shen, J.; Lin, G.; Dong, H.; Li, K.; Zhou, Q. Analysis of main causes of deaths and potential years of life lost among residents in Guangzhou City, 2011. *South China. J. Prev. Med.* **2013, 39**, 15–19.
28. Municipality, S.B. Guangzhou Statistical Yearbook. Available online: http://data.gzstats.gov.cn/gzStat1/chaxun/njsj.jsp (accessed on 22 April 2017).
29. Lin, D.; Zeng, F. Analysis on the life expectancy in Guangzhou. *J. Sun Yat-sen Univ.* **1995**,35, 55–62.
30. Yang, M.; Bi, Z.; Ren, C.; He, X.; Tang, N.; Lin, H.; Wen, Y.; Shi, S.; Wu, R. The Life Expectancy in Guangzhou Approaches 80 Years. *Guangzhou Daily*, 27 December 2011.
31. Li, X. The Life Expectancy of People in Guangzhou Reaches 81.72 Years. *Nanfang Daily*, 15 March 2017.
32. Raftery, A.E.; Chunn, J.L.; Gerland, P.; Ševčíková, H. Bayesian probabilistic projections of life expectancy for all countries. *Demography* **2013**, *50*, 777–801.
33. Leridon, H. Demography: Measuring and Modeling Population Processes. *Population* **2001**, *57*, 591.
34. Field, C.B.; Barros, V.R.; Dokken, D.J.; Mach, K.J.; Mastrand rea, M.D.; Bilir, T.E.; Chatterjee, M.; Ebi, K.L.; Estrada, Y.O.; Genova, R.C.; et al. *IPCC, 2014: Climate Change 2014: Impacts, Adaptation, and Vulnerability. Part A: Global and Sectoral Aspects*; Contribution of Working Group II to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change; Cambridge University Press: Cambridge, UK; New York, NY, USA, 2014.

35. Yang, C.; Meng, X.; Chen, R.; Cai, J.; Zhao, Z.; Wan, Y.; Kan, H. Long-term variations in the association between ambient temperature and daily cardiovascular mortality in Shanghai, China. *Sci. Total Environ.* **2015**, *538*, 524–530.
36. Petkova, E.P.; Gasparrini, A.; Kinney, P.L. Heat and Mortality in New York City since the Beginning of the 20th Century. *Epidemiology* **2014**, *25*, 554–560.
37. Barrett, J.R. Increased minimum mortality temperature in France: Data suggest humans are adapting to climate change. *Environ. Health Perspect.* **2015**, *123*, A184.
38. Todd, N.; Valleron, A.-J. Space-time covariation of mortality with temperature: A systematic study of deaths in France, 1968–2009. *Environ. Health Perspect.* **2015**, *123*, 659–664.
39. Gasparrini, A.; Armstrong, B.; Kenward, M.G. Distributed lag non-linear models. *Stat. Med.* **2010**, *29*, 2224–2234.
40. Peng, R.D.; Dominici, F.; Louis, T.A. Model choice in time series studies of air pollution and mortality. *J. R. Stat. Soc. Ser. A Stat. Soc*. **2006**, *169*, 179–203.
41. Liu, T.; Zhang, Y.H.; Xu, Y.J.; Lin, H.L.; Xu, X.J.; Luo, Y.; Xiao, J.; Zeng, W.L.; Zhang, W.F.; Chu, C. The effects of dust–haze on mortality are modified by seasons and individual characteristics in Guangzhou, China. *Environ. Pollut.* **2014**, *187*, 116–123.
42. Liu, T.; Li, T.T.; Zhang, Y.H.; Xu, Y.J.; Lao, X.Q.; Rutherford, S.; Chu, C.; Luo, Y.; Zhu, Q.; Xu, X.J.; et al. The short-term effect of ambient ozone on mortality is modified by temperature in Guangzhou, China. *Atmos. Environ.* **2013**, *76*, 59–67.
43. Zeng, Y.; Hesketh, T. The effects of China's universal two-child policy. *Lancet* **2016**, *388*, 1930–1938.
44. Zeng, Y.; Wang, Z. A Policy Analysis on Challenges and Opportunities of Population/Household Aging in China. *J. Popul. Age* **2014**, *7*, 255–281.
45. United Nations Human Settlements Programme. *Cities and Climate Change: Global Report on Human Settlements 2011*; Earthscan Ltd, London, UK, 2011.
46. Kovats, R.S.; Hajat, S. Heat Stress and Public Health: A Critical Review. *Ann. Rev. Public Health* **2008**, *29*, 41–55.
47. Jenkins, K.; Hall, J.W.; Glenis, V.; Kilsby, C.G.; Mccarthy, M.P.; Goodess, C.M.; Smith, D.; Malleson, N.; Birkin, M. Probabilistic spatial risk assessment of heat impacts and adaptations for London. *Clim. Chang.* **2014**, *124*, 105–117.
48. Matthies, F.; Bickler, G.; Marín, N.C.; Hales, S. *Heat-Health Action Plans*; World Health Organization: Copenhagen Ø, Denmark, 2008; pp. 1–55.
49. Gosling, S.N.; McGregor, G.R.; Lowe, J.A. Climate change and heat-related mortality in six cities Part 2: Climate model evaluation and projected impacts from changes in the mean and variability of temperature with climate change. *Int. J. Biometeorol.* **2009**, *53*, 31–51.
50. Anderson, B.G.; Bell, M.L. Weather-related mortality: How heat, cold, and heat waves affect mortality in the United States. *Epidemiology* **2009**, *20*, 205–213.

2.7 Effects of extreme temperatures on mortality and hospitalization in Ho Chi Minh City, Vietnam

Tran Ngoc Dang [1,2,*], Yasushi Honda [3], Dung Van Do [2], Anh Lan Thi Pham [2], Cordia Chu [4], Cunrui Huang [5] and Dung Phung [5,6,*]

[1] Institute of Research and Development, Duy Tan University, Da Nang 550000, Vietnam
[2] Faculty of Public Health, University of Medicine and Pharmacy in Ho Chi Minh City, Ho Chi Minh 70000, Vietnam; dvdung@ump.edu.vn (D.V.D.); lanh2804@gmail.com (A.L.T.P.)
[3] Faculty of Health and Sport Sciences, University of Tsukuba, Tsukuba 305-8577, Japan; honda.yasushi.fn@u.tsukuba.ac.jp
[4] Centre for Environment and Population Health, Griffith University, Brisbane 4001, Australia; c.chu@griffith.edu.au
[5] School of Public Health, Sun Yat-sen University, Guangzhou 510000, China; huangcr@mail.sysu.edu.cn
[6] School of Medicine, Nathan Gold Coast Campus, Griffith University, Nathan QLD 4111, Australia
* Correspondence: ngocdangytcc@gmail.com (T.N.D); d.phung@griffith.edu.au (D.P.); Tel.: +84-985-137-435 (T.N.D.); +61-737-355-078 (D.P.)

Dang TN, Honda Y, Van Do D, Pham ALT, Chu C, Huang C, et al. Effects of Extreme Temperatures on Mortality and Hospitalization in Ho Chi Minh City, Vietnam. International Journal of Environmental Research and Public Health 2019;16(3):432.

Abstract: There is a lack of research focusing on the association of temperature with mortality and hospitalization in developing countries with tropical climates and a low capacity to cope with the influences of extreme weather events. This study aimed to examine and compare the effect of temperature, including heat waves, on mortality and hospitalization in the most populous city of Vietnam. We used the quasi-Poisson time series regression coupled with the distributed lag non-linear model (DLNM) to examine the overall pattern and compare the temperature-health outcome relationship. The main and added effects of heat waves were evaluated. The main effect of heat waves significantly increased the risk of all cause-specific mortality. Significant main effects of heat waves on hospitalization were observed only for elderly people and people with respiratory diseases (elderly, relative risk (RR) = 1.28, 95% confidence interval (CI) = 1.14–3.45; respiratory diseases, RR = 1.3, 95% CI = 1.19–1.42). The RRs of the main effect was substantially higher than those of the added effect in mortality; the same was applicable for hospitalizations of people with respiratory diseases and elderly people. The findings of this study have important implications for public health adaptation and prevention program implementation in the protection of residents from the adverse health effects of temperature.

Keywords: temperature-related mortality; temperature-related hospitalization; main effect; added effect; heatwaves; Vietnam

Introduction

Global warming, a phenomenon of climate change, the rate of which has been accelerated by increasing anthropogenic greenhouse gas emissions, is contributing to a higher frequency, intensity, and duration of extreme weather events, such as heat waves [1]. High temperatures are significantly associated with both morbidity [2–4] and mortality [5–8], and the associated adverse health outcomes encompass a wide range of communicable [9–13] and non-communicable diseases [14–17]. The impact of high temperatures is substantially amplified in megacities with large populations and building densities due to the thermal properties of the built environment (the so-called urban heat island phenomenon).

Studies in temperature–health effects are still open to fulfilling a couple of knowledge gaps. First, while there is sufficient evidence on the effect of high temperatures on mortality, worldwide, the evidence on the effect of high temperatures on hospitalization is less conclusive [18]. For instance, studies have demonstrated that high temperatures are associated with increases in the rates of hospital admission due to cardiorespiratory diseases in several cities in the United States of America (USA) [15,19,20]. However, the relationship between high temperatures and cardiovascular disease (CVD) admissions was not significant in some European cities [3,21,22] and some cities in the USA [23]. Second, the contrasting pattern of CVD hospitalizations and mortality about heat waves raised a hypothesis that deaths due to CVD occur rapidly among people before they reach a hospital [24]. However, most of the studies mentioned above used different analytic methods and populations; therefore, it is difficult to compare the results. It is important to conduct further studies to examine the hypothesis using data on mortality and hospitalization from the same population and to apply the same statistical analyses for comparison. The contrasting patterns of CVD hospitalization and mortality in relation to heat also open the question "Do the patterns of different types of diseases (e.g., cardiovascular, respiratory) and different population characteristics (e.g., men, women, elderly people, etc.) vary in response to different types of heat (e.g., high temperature and heat waves)?". Finally, most previous studies in this context were implemented in developed countries with a temperate climate. There is a lack of research on the relationship of temperature with mortality and hospitalization in developing countries that have a tropical climate and a low capacity to cope with the influences of extreme weather events [4,21,25,26], even though a non-uniform spatial pattern in heat-related health risk has been strongly theoretically supported based on a previous study [2].

This study aims to examine the main and added effects of heat waves on mortality and hospitalization. In addition, we also compare the relationship between heat-mortality and heat-hospitalization.

Materials and Methods

Study Area

Ho Chi Minh City (HCMC) is located in the south of Vietnam and has a "tropical wet and dry" climate (Köppen-Geiger classification). HCMC experiences a high annual average temperature and two distinct seasons: a rainy season and a dry season. The rainy season usually lasts from May to November, with an average rainfall of about 1800 mm during the season, and about 150 rainy days per year [27]. The dry season extends from December to April, and the period with the highest temperature is from March to May (i.e., sometimes March-May is considered 'summer' in HCMC). The annual average temperature is 28 °C, with few variations throughout the year, and the city experiences between 2400 and 2700 h of sunshine per year [27]. HCMC is one of the most populous cities in Vietnam, with a total population of more than 7 million, accounting for 8.4% of the total population of Vietnam; the population density is approximately 2660 people per km^2 [28].

Data Source and Quality

Daily mortality data from 322 community health centres in 24 districts of HCMC were collected from the national system (the A6 mortality reporting system) from 1 January 2010 to 31 December 2013. The A6 mortality system has been described elsewhere [29]; data from this system have been validated in previous studies and showed good completeness and accuracy, particularly in regard to circulatory disease, cancer, and injury cases [30,31]. The final mortality data in this study included 101,959 decedents, with information on the date of death, sex, age, and cause of death as classified by the 10th Revision of the International Classification of Disease (ICD10) code. In this study, cause-specific mortality included CVDs (i.e., ICD10 code I00-99) and respiratory diseases (i.e., ICD10 code J00-99).

Data on hospital admissions included daily counts for non-external causes, CVDs (I00-99; excluding acute rheumatic fever, I00-02, and chronic rheumatic heart diseases, I05-09), and respiratory diseases (J00-99; excluding lung diseases due to external agents, J60-70). We obtained admission data for the period from 1 January 2010 to 31 October 2013 from the hospital records of the two largest hospitals in HCMC: Gia Dinh People's Hospital and 115 People's Hospital. These multi-faculty hospitals have 1200 and 1600 beds, respectively. Data extracted from the admission records included those on primary and discharge diagnoses (ICD-10 codes), date of admission, date of discharge, age, sex, and the district of residence of individual patients. To avoid exposure to misclassification, patients from locations other than HCMC were excluded.

Daily weather data were obtained from the National Oceanic and Atmospheric Administration's National Climate Data Center for the same period with mortality and hospitalization data. The data comprise those on daily minimum, average, and maximum temperatures (°C), and relative humidity (%) collected at the Tan Son Nhat airport weather monitoring station [32].

This study was approved by the Griffith University Human Research Ethics Committee (GU Ref No: ENV/23/15/HREC) and a support letter from the Health Environment Management Agency, Vietnam Ministry of Health (No: 937/MT-SKCĐ, 2013).

Definition of a Heat Wave

While there is no global consensus on the definition of a 'heat wave', it is commonly defined as a few consecutive days with high temperatures above a certain threshold [34]. In this study, heat waves were defined using a combination of intensity (≥97th percentile of the daily average temperature, i.e., 30.9 °C) and duration (≥2 consecutive days). This definition is consistent with that used in some previous studies [34,35].

Several recent studies have described the heat wave effect as a sum of two contributions: the intensity effect due to the independent effects of daily hot temperatures (i.e., main effect), and the duration effect due to sustained heat wave days (i.e., added effect) [34,36,37]. Therefore, in this study, we examined both the main and added effects of heat waves on mortality and hospitalization using a time series regression model, as shown in detail below.

Statistical Model

We used a quasi-Poisson time series regression model linking daily mortality or daily hospitalization (i.e., outcomes or responses) with daily average temperature (i.e., exposure) [38]. To control for long-term trends and seasonality, we used a natural cubic spline function of time with 7 degrees of freedom (df) per year. In addition, to account for the potential non-linear relation between temperatures and health outcomes, we applied a distributed lag non-linear model (DLNM) using a cross-basis function of multiple lag-day temperatures [39,40]. The parameters of this cross-basis function followed the specifications indicated in a previous study [41], which included a quadratic B-spline with two internal knots placed at equally spaced values of the temperature in the exposure−response dimension, and a natural cubic B-spline with an intercept and three internal knots placed at equally spaced values of the log scale of lags in a lag-response dimension. The allowed maximum lags in this study were up to 7 days, because the hot temperature effects were acute and possibly affected by mortality displacement [42]. To examine the independent effects of heat waves (i.e., main and added effects) on outcomes, we introduced into the model at the same time the continuous average temperature variable and the heat wave indicator variable that has two values: '1' if a heat wave occurred and '0' if otherwise. The general model is:

$$Yt \sim \text{quasi-Poisson } (\mu t)$$

$$\text{Log } (Yt) = \alpha + \beta 1 * Tt,l + \beta 2 * HW + \beta 3 * DOW + \beta 4 * NCS \text{ (Time, 7 df/year)} \quad (8)$$

where Yt denotes the daily count of outcomes (mortality or hospitalization) on day t; l signifies the lag days; Tt,l signifies a matrix obtained by applying the "cross-basis" DLNM functions to the mean temperature; HW is a heat wave indicator (i.e., '1' if a heat wave, otherwise '0'); DOW signifies the day of the week; NCS is a natural cubic spline function; and Time is a variable that takes consecutive numbers from '1' on the first day of observation to '1461' on the final day within the observation period (2010–2013).

The main effect of heat waves was then calculated as the relative risk (RR) of the median value of temperature distribution among heat wave days (HW = 1) compared to the minimum mortality/or hospitalization temperature (MMT) (i.e., the temperature at which the risk is lowest). The added effect of heat waves was calculated as the RR between heat wave days and non-heat wave days (i.e., exp(β2) in Equation (1)).

We also performed sensitivity analyses to test these modelling choices, in which we simplified the lag structure by fitting the moving average of temperature series over lag 0–1,0–3, and 0–7 days and changing the number of knots for temperature and lag days; and performed sensitivity analyses with different heat wave intensity definitions (i.e., 97th, 98th, and 99th percentile) and duration (i.e., 2 days, 4 days). All analyses were performed using R software 3.2.2., the "dlnm" package [40]. The R code to reproduce the results of this study can be obtained by contacting the first author.

Results

Descriptive Statistics

The total mortality count from 2010 to 2013 in HCMC was 101,959, including 22,218 cases (21.8%) attributed to CVDs, and 8804 (8.63%) to respiratory diseases. A large proportion of the deceased people were older than 65 years, accounting for 58.2% of all deaths. The mortality values in the male and female cases were 54.6% and 45.4% respectively. A total of 310,045 all-cause hospitalizations were recorded during the study period. The highest proportion (70%) of hospitalizations were attributed to elderly people, while a higher proportion of female patients than male patients were hospitalized (51.8% vs. 48.2%). On average, the all-cause daily mortality and daily hospitalization values were 70 and 221 cases, respectively. Table 1 shows the descriptive statistics of daily weather condition, daily mortality, and daily hospitalization.

The weather in HCMC was hot year-round, with a mean daily average temperature of 28.4 °C, ranging from 23 to 32 °C. Table 2 displays data on the intensity and duration of the heat waves in HCMC during the study period. The longest heat wave lasted 16 days from 5–21 May 2010, in which the median temperature was 31.75 °C, ranging from 30.95 to 32.1 °C.

Table 1. Summary statistics of daily weather conditions, daily mortality, and daily hospitalization in Ho Chi Minh City, Vietnam, 2010–2013.

Variables	**Mean**	**Standard Deviation**	**Minimum**	**Percentile**			**Maximum**
				25%	**50%**	**75%**	
Maximum temperature (°C)	33.8	1.8	24.5	32.7	34	35	39
Average temperature (°C)	28.4	1.3	23.0	27.5	28.4	29.4	32.1
Minimum temperature (°C)	25.4	1.4	20.0	24.5	25.4	26.3	29.8
Average relative humidity (%)	74.1	7.2	52	70	74	79	94
Mortality data #							
All-cause	70	11.5	26	62	70	77	111
Cardiovascular disease	15	4.3	3	12	15	18	34
Respiratory disease	6.0	2.6	0	4	6	8	16
Male	38	7.3	13	33	38	43	64
Female	32	7.1	10	27	31	36	59
0–14 years old	1	1.0	0	0	1	2	5
15–64 years old	28	5.8	6	24	28	32	46
≥65 years old	41	8.6	14	25	40	46	71
Hospitalization data #							
All-cause	222	52.3	83	175.8	224	258	456
Cardiovascular disease	42	9.3	18	35	42	48	76
Respiratory disease	25	7.1	7	20	24	30	49
Male	107	25.2	36	87	105	123	239
Female	115	29.4	26	89	116	136	220
0–14 years old	11	3.7	1	8	10	13	24
15–64 years old	56	15.1	19	44	55	66	112
≥65 years old	155	38.3	52	123	155	182	327

the unit of mortality and hospitalization is the number of cases per day.

Table 2. Intensity and duration of heat waves in Ho Chi Minh City, 2010–2013.

Heat Wave Definition (Threshold, Duration)	Start–End Date	Duration (Days)	Intensity (°C) Median (Range)
97th percentile, 2 days	24/4–26/4/2010	2	31.2 (31.07–31.25)
	5/5–21/5/2010	16	31.75 (30.95–32.1)
	23/5–27/5/2010	4	31.125 (30.925–32.125)
	30/5–2/6/2010	3	31.23 (31.025–31.3)
	31/3–6/4/2013	6	31.4 (30.9–32)

Figure 1 shows the time series plot of the daily basis of all-cause mortality, all-cause hospitalization, and temperature. In the summer months in 2010 and 2013, the temperatures were very high (i.e., on average above 31 °C, and sometimes reached 32 °C), indicating that heat waves occurred during these periods. The observed daily mortality counts were also high during the summer months in 2010 and 2013; this implies the heat wave occurrence increased the mortality risk. The effect of heat waves on hospitalization, however, was not obvious.

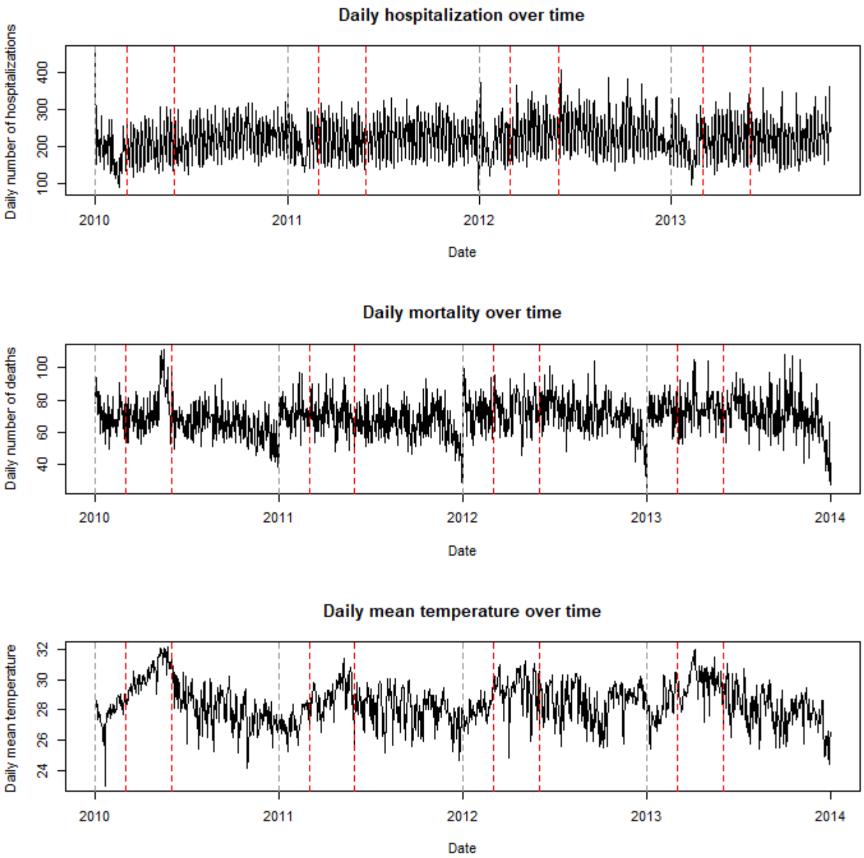


Figure 1. Time series plot of the daily basis of all-cause mortality, all-cause hospitalization, and temperature in Ho Chi Minh City from 2010 to 2013. The red lines indicate the summer period from March to May.

The Short-Term Relationship between Temperature and Health Outcomes

The overall short-term associations between mortality, hospitalization, and temperature are shown in Figure 2. The temperature-mortality relationship appeared J-shaped with an MMT of 29.4 °C (i.e., temperatures above 29.4 °C increased the risk of mortality), whereas the temperature–hospitalization relationship showed a modest increase in the risk of hospitalization at very high temperatures (the increase was not statistically significant). The hot effect was acute for mortality (the effect of 31 °C occurred on day 0 and lasted two days), whereas the hot effect was neither acute nor significant for hospitalization.

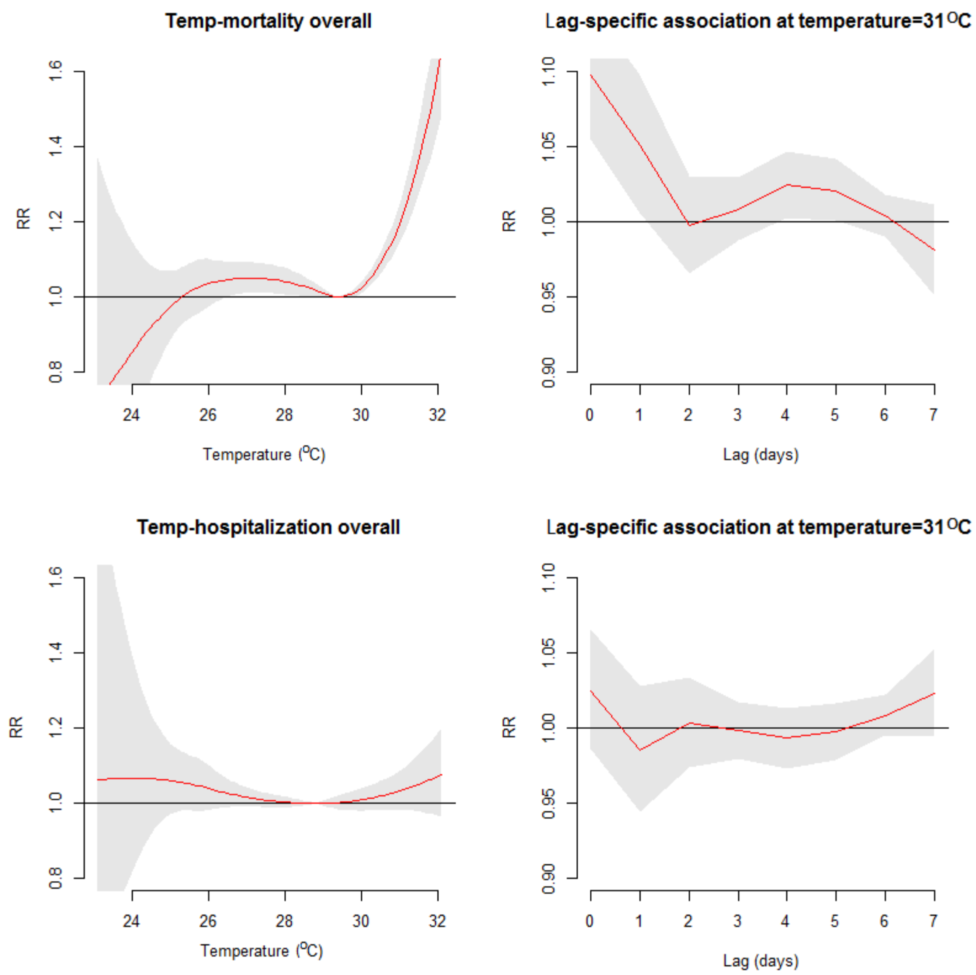


Figure 2. Short-term association between all-cause mortality, all-cause hospitalization, and temperature. The red curves indicate cumulative relative risk (RR), and the grey areas indicate 95% confidence intervals.

We performed sensitivity analyses to check the robustness of the model. The alternative models for the lag structure are shown in Figure S1 for mortality and Figure S2 for hospitalization, and alternative models for a number of knots for temperature and lag days are shown in Figure S3. The overall temperature–mortality and temperature–hospitalization curves of the alternative models were relatively similar (especially in terms of the heat-related association), implying that our results are robust and unlikely to be affected by the modelling choices.

Comparability of the Temperature Effects on Mortality and Hospitalization

The main and added effects of heat waves are presented in Figure 3. It was observed that the main effect of heat waves significantly increased the risk of mortality in all categories, in which the RRs were the highest for the mortality of people with respiratory diseases and elderly people (respiratory mortality, RR = 1.45, 95% confidence interval (CI) = 1.25–1.70; elderly people mortality, RR = 1.43, 95% CI = 1.34–1.53). The main effect of heat waves on hospitalization, however, was only significant for the hospitalizations of people with respiratory diseases and elderly people (respiratory hospitalization, RR = 1.3, 95% CI = 1.19–1.42; elderly people hospitalization, RR = 1.28, 95% CI = 1.14–3.45). The RRs of the main effect was substantially higher than those of the added effect in mortality; the same was applicable to hospitalizations of people with respiratory diseases and elderly people. We observed elevated risks of the added effect in hospitalization in both the male and female groups (male hospitalization, RR = 1.06, 95% CI = 1.01–1.12; female hospitalization, RR = 1.08, 95% CI = 1.03–1.14), but only elevated risks of the added effect in mortality in the female group (female mortality, RR = 1.11, 95% CI = 1.04–1.18). It is worth noting that the added effect was significant in the hospitalization group with younger age, but not significant in the mortality group with younger age (0–64 years at hospitalization, RR = 1.08, 95% CI = 1.03–1.13).

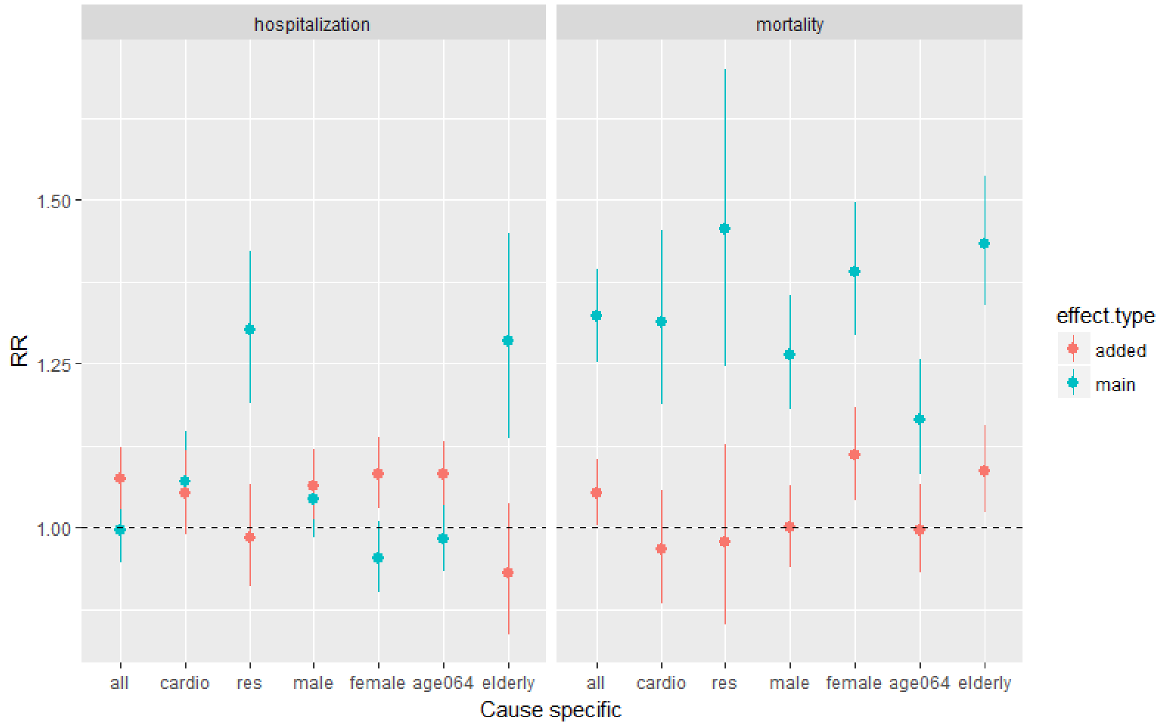


Figure 3. Main and added effect of heat waves on hospitalization and mortality cause specific. The left panel is for hospitalization and the right panel is for mortality. The blue point is the RRs of main effects with 95% confidence intervals and the red point is the RRs of added effects with 95% confidence intervals.

The sensitivity results of the different heat wave definitions are shown in Figure S4 for mortality and Figure S5 for hospitalization. The patterns of the main and added effects of the heat waves were quite consistent across the definitions, indicating that the results are unlikely to be affected by the heat wave definitions.

Discussion

This is the first comprehensive study to examine the effects of temperatures on health outcomes using both mortality and hospitalization data in Vietnam. The study reports findings on the patterns of the temperature–health risk relationship. Overall, the results of this study revealed that increased temperatures above the threshold of 29 °C were associated with an elevated risk of mortality but not hospitalization. The same applied to the main effect of temperature (i.e., intensity effect) during heat waves, except in the case of elderly people and people with respiratory diseases. In the same geographical area, despite a lack of studies on mortality, a study conducted by Phung et al. (2016) illustrated that 1 °C increases in the average temperature were associated with 1.3% increases in the risk of hospital admission for all causes in the Mekong Delta region [18]; significant effects of temperature were observed in hospital admissions due to infectious and respiratory diseases. However, the relationship between temperature and CVD admission was insignificant in that study, similar to the findings of our study. The discrepancy in the magnitude of risk between hospitalizations and mortality during heat waves has been reported in other regions as well. For example, during the 1995 Chicago heat waves, the all-cause mortality increased by 147%, whereas the hospital admission rate increased by only 11% [43]. In Greater London, the United Kingdom, during the 1995 6-day heat wave, the daily mortality values rose by 10.8% (95% CI 2.8 to 19.3), while the daily hospitalization rate increased by 2.6% (95% CI −2.2 to 7.6) [44]. This discrepancy may be attributed to the fact that many deaths occur rapidly or among isolated people before they reach the hospital during heat waves [24,44]. In the Chicago heat waves, many deaths were observed among people living alone or who had a lack of social contacts [45]. The presence of working home air-conditioning, taking extra showers, using fans, and visiting cool environments are associated with a lower risk of death during heat waves [46]. A study conducted by Nitschke et al. found that the total mortality, as well as disease- and age-specific mortality values, did not increase during heat waves in Adelaide, potentially due to the high prevalence of air conditioning (82%) [47]. In HCMC, the discrepancy between mortality and hospitalization during heat waves indicates that the population is currently not well-adapted to heat waves. There is a need for further studies investigating the specific factors associated with a higher risk of death during heat waves, and to provide potential risk-reducing interventions in the setting of heat waves in HCMC.

This study also revealed that the main effect of heat waves (i.e., intensive effect) was stronger than the added effect in mortality. This result is similar to that observed in a study conducted in 108 communities in the USA, in which the added effect was small and only apparent after 4 consecutive days [34]. Another study in the four communities of Guangdong province, China, found that the main effect was greater than the added effect (i.e., 8.2% vs. 0%) [37]. Our results have implications for the heat-health warning system (HWS) in HCMC. It is very important for the HWS to provide alerts on days with high temperatures when heat waves occur rather than basing alerts on the duration of the heat waves. However, the added effects of heatwave were significant for elderly and female mortality. Therefore, for vulnerable groups (i.e., elderly and female populations) the alerts of HWS based on duration of the heat waves are also important to prevent deaths from heatwaves even if/when the temperatures are not so high during the heatwaves.

The significant positive relationship observed between temperature and the risk of respiratory disease and elderly people-related mortality and hospitalization can be explained by some possible mechanisms, although the causal effect of this relationship is not well understood. First, it is known that chronic obstructive pulmonary disease (COPD) exacerbations are among the most common reasons for respiratory disease admissions among elderly people [48]. These acute episodes are associated with airway and systemic inflammation as well as cardiovascular comorbidity and may be facilitated by heat exposure. Under extremely hot weather conditions, COPD patients may hyperventilate [49], increasing the possibility of dynamic hyperinflation, leading to dyspnea and mechanical and cardiovascular effects. Moreover, elderly people with COPD may be unable to dissipate excess heat through circulatory adjustment, and exposure to high temperatures may lead to the risk of developing pulmonary vascular resistance secondary to the peripheral pooling of blood or hypovolemia [49]. The underlying mechanism of the temperature–respiratory health relationship should be further studied for a better understanding of the pathophysiology and clinical course of heat-related illness. The findings of this study are in line with this possible mechanism since the highest effects of temperature were observed among elderly people.

This study has some limitations. First, while the mortality data are considered to be representative of the research location, the hospital admission data were obtained from two multi-faculty hospitals, which may not reflect the hospitalizations of the whole city. Moreover, these hospitals provide a higher level of curative treatment, so minor cases that were admitted to private clinics or lower-level hospitals (i.e., district hospitals) may have been missed. Second, this study could not examine the effects of high temperatures on individual cause-specific diseases, focusing instead on groups of diseases (all-cause, respiratory diseases, and CVDs) due to the limited number of cases. A previous study [18] indicated that temperature may have different effects by disease type, especially in the case of CVDs. For example, a study by Konken et al. (2003) illustrated that high temperatures were associated with an increased risk of hospital admissions for acute myocardial infarction and congestive heart failure but also with a decreased admission rate due to coronary atherosclerosis and pulmonary heart disease. Thus, combining all CVDs may have attributed to the decreased sensitivity in the relationship between temperature and CVD in this study. Third, this study failed to examine the modification effects of individual-level socioeconomic factors such as information on adaptive measures (e.g., air conditioning), occupation, or how much time people spent outdoors, which may reflect the actual exposure to high ambient temperatures. However, these factors may not change in a short period, as daily time series were used to examine temperature–health outcomes in this study. Finally, we did not control the effects of wind and air pressure (due to the lack of data) in the association between high temperature and mortality and hospitalization. Future studies should consider other weather factors (i.e., wind, air pressure) in examining the association between high temperature and health outcomes.

Conclusions

This study provided evidence revealing that while high temperatures significantly increase the risks of both mortality and hospitalizations for respiratory diseases, heat waves result in a significantly elevated risk of mortality among residents in the most populous city in Vietnam. In the comparison of effect magnitude, the heat-morbidity risk was less sensitive and certain than the heat-mortality risk. Future studies with larger-scale hospitalization data should be implemented to further examine the utility and sensitivity of admission data in terms of heat-health risk; it is also warranted to consider advanced methods that better model the uncertainty and overdispersion nature of time series data in further studies. HCMC is highly vulnerable to climate change; extreme temperature conditions, under interaction with other factors such as air pollution and socio-demographic factors (e.g., high population density), have been anticipated to more frequently occur in this city. Therefore, our findings have important implications for the projected impact on residents. Public health adaptation and prevention programs such as developing early warnings and response plans, improving the capacity of healthcare systems to adapt to climate change-related extreme weather events, educating community members to minimize the effects of high temperatures, and establishing temperature shelters in residential hot spots should be implemented to protect residents from this additional burden of adverse health effects.

References

1. Barros, V.R.; Field, C.B.; Dokken, K.J.; March, M.D.; Mastrandrea, T.E.; Bilir, M.; Chatterjee, K.L.; Ebi, Y.O.; Estrada, J.C.; et al. *Climate Change 2014: Impacts, Adaptation and Vulnerablity. Contribution of Working Group II to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change*; Cambridge University Press: Cambridge, UK, 2014.
2. Hondula, D.M.; Barnett, A.G. Heat-Related Morbidity in Brisbane, Australia: Spatial Variation and Area-Level Predictors. *Environ. Health Perspect*. **2014**, *122*, 831–836.
3. Michelozzi, P.; Accetta, G.; Desario, M.; D'Ipolliti, A.; Marino, C.; Baccini, M.; Biggeri, A.; Anderson, H.R.; Katsouyanni, K.; Ballester, F.; et al. High temperature and hospitalizations for cardiovascular and respiratory causes in 12 European cities. *Am. Respir. Crit. Care Med*. **2009**, *179*, 383–389.
4. Phung, D.; Guo, Y.; Thai, P.; Rutherford, S.; Wang, X.; Nguyen, M.; Do, C.M.; Nguyen, N.H.; Alam, N.; Chu, C. The effects of high temperature on cardiovascular admissions in the most populous tropical city in Vietnam. *Environ. Pollut*. **2015**, *208*, 33–39.
5. Guo, Y.; Gasparrini, A.; Amstrong, B.; Li, S.; Tawatsupa, B.; Tobias, A.; Laviqne, E.; Coelho, M.d.Z.S.; Leone, M.; Pan, X.; et al. Global variation in the effects of ambient temperature on mortality: A systematic evaluation. *Epidemiology* **2014**, *25*, 781–789.
6. Gasparrini, A.; Guo, Y.; Hashizume, M.; Laviqne, E.; Anobetti, A.; Swartz, J.; Tobias, A.; Tong, S.; Rocklov, J.; Forsberg, B.; et al.: Mortality risk attributable to high and low ambian temperature: A multicountry observational study. *Lancet* **2015**, *386*, 369–375.
7. Huang, C.; Barnett, A.G.; Wang, X.; Tong, S. Effects of extreme temperatures on years of life lost for cardiovascular deaths: A time-series study in Brisbane, Australia. *Circulation* **2012**, *5*, 609–614.
8. Yang, X.; Li, L.; Wang, J.; Huang, J.; Lu, S. Cardiovascular mortality associated with low and high temperatures: Determinants of inter-region vulnerability in China. *Int. J. Environ. Res. Public Health* **2015**, *12*, 5918–5933.
9. Xiang, J.; Hansen, A.; Liu, Q.; Liu, X.; Tong, M.X.; Sun, Y.; Cameron, S.; Hanson-Easay, S.; Han, G.S.; Williams, C.; et al. Association between dengue fever incidence and meteorological factors in Guangzhou, China, 2005–2014. *Environ. Res*. **2017**, *153*, 17–26.
10. Phung, D.; Huang, C.; Rutherford, S.; Chu, C.; Wang, X.; Nguyen, M.; Nguyen, N.H.; Manh, C.D.; Nguyen, T.H. Association between climate factors and diarrhoea in a Mekong Delta area. *Int. J. Biometeorol*. **2015**, *59*, 1321–1331.
11. Nguyen, H.X.; Chu, C.; Nguyen, H.L.; Nguyen, H.T.; Manh, C.D.; Rutherford, S.; Phung, D. Temporal and spatial analysis of hand, foot, and mouth disease in relation to climate factors: A study in the Mekong Delta region. *Vietnam. Sci. Total Environ*. **2017**, *581*, 766–772.
12. Milazzo, A.; Giles, L.C.; Zhang, Y.; Koehler, A.P.; Hiller, J.E.; Bi, P: The effect of temperature on different Salmonella serotypes during warm seasons in a Mediterranean climate city, Adelaide, Australia. *Epidemiol. Infect*. **2016**, *144*, 1231–1240.
13. Yang, D.; Xu, C.; Wang, J.; Zhao, Y. Spatiotemporal epidemic characteristics and risk factor analysis of malaria n Yunnan Province, China. *BMC Public Health* **2017**, *17*, 66.
14. Ebi, K.L.; Exuzides, K.A.; Lau, E.; Kelsh, M.; Barnston, A. Weather changes associated with hospitalizations for cardiovascular diseases and stroke in California, 1983–1998. *Int. J. Biometeorol*. **2004**, *49*, 48–58.
15. Schwartz, J.; Samet, J.M.; Patz, J.A. Hospital admission for heart disease: The effects of temperature and humidity. *Epidemiology* **2004**, *15*, 755–761.
16. Bayentin, L.; Adlouni, S.E; Ouarda, T.B; Gosselin, P.; Doyon, B.; Chebana, F. Spatial variability of climate effects on ischemic heart disease hospitalization rates for the period 1989–2006 in Quebec, Canada. *Int. J. Health Geogr*. **2010**, *9*, 5.

17. Turner, L.R.; Barnett, A.G.; Connell, D.; Tong, S: Ambient temperature and cardiorespiratory morbidity: A systematic review and meta-analysis. *Epidemiology* **2012**, *23*, 594–606.
18. Phung, D.; Guo, Y.; Nguyen, H.T.L.; Rutherford, S.; Baum, S.; Chu, C. High temperature and risk of hospitalizations, and effect modifying potential of socio-economic conditions: A multi-province study in the tropical Mekong Delta Region. *Environ. Int*. **2016**, *92*, 77–86.
19. Konken, P.J.; Piver, W.T.; Ye, F.; Elixhauser, A.; Olsen, L.M.; Portier, C.J Temperature, air pollution, and hospitalization for cardiovascular diseases among elderly people in Denver. *Environ. Health Perspect*. **2003**, *111*, 1312–1317.
20. Lin, S.; Luo, M.; Walker, R.J.; Liu, X.; Hwang, S.A.; Chinery, R. Extreme high temperatures and hospital admissions for respiratory and cardiovascular diaseas. *Epidemiology* **2009**, *20*, 738–746.
21. Kovats, R.S.; Edwards, S.J.; Hajat, S.; Armstrong, B.G.; Ebi, K.L.; Menne, B.; Grp, C. The effect of temperature on food poisoning: A time-series analysis of salmonellosis in ten European countries. *Epidemiol. Infect*. **2004**, *132*, 443–453.
22. Linares, C.; Diaz, J. Impacts of high temperature on hospital admissions: Comparative analysis with previous studies about mortality (Madrid). *Eur. J. Public Health* **2008**, *18*, 317–322.
23. Gronlund, C.J.; Zanobetti, A.; Schwartz, J.D.; Wellenius, G.A.; O'Neill, M.S. Heat, heat waves, and hospital admissions among the elderly in the United States, 1992–2006. *Environ. Health Perspect*. **2014**, *122*, 1187–1192.
24. Mastrangelo, G.; Hajat, S.; Fadda, E.; Buja, A.; Fedeli, U.; Spolaore, P. Contrasting patterns of hospital admissions and mortality during heat waves: Are deaths from circulatory disease a real excess or an artifact? *Med. Hypotheses* **2006**, *66*, 1025–1028.
25. Basu, R. High ambient temperature and mortality: A review of epidemiologic studies from 2001 to 2008. *Environ. Health* **2009**, *8*, 40.
26. Hosking, J.; Jones, R.; Percival, T.; Turner, N.; Ameratunga, S. Climate change: The implications for children health in Australasia. *J. Paediatr. Child Health* **2010**, *47*, 493–496.
27. Viet Nam: Ha Noi and Ho Chi Minh City Power Grid Development Sector Project. Available online https://www.adb.org/sites/default/files/linked-documents/46391-001-ieeab-04.pdf (accessed on 1 November 2018).
28. Guo, Y.; Li, S.; Chen, D.; Williams, G.; Tong, S. Projecting future temperature-related mortality in three largest Australian cities. *Environ. Pollut*. **2016**, *208*, 66–73.
29. Dang, T.N.; Seposo, X.T.; Duc, N.H.C.; Thang, T.B.; An, D.D.; Hang, L.T.M.; Long, T.T.; Loan, B.T.H.; Honda, Y. Characterizing the relationship between temperature and mortality in tropical and subtropical cities: A distributed lag non-linear model analysis in Hue, Viet Nam, 2009–2013. *Glob. Health Act.* **2016**, *9*, 28738, doi:10.3402/gha.v9.28738.
30. Stevenson, M.R.; Ngoan, L.T.; Hung, D.V.; Huong, Tu, N.T.; Mai, A.L; Ivers, R.Q.; Huong, H.T. Evaluation of the Vietnamese A6 mortality reporting system: Injury as a cause of death. *Inj. Prev*. **2012**, *18*, 360–364.
31. Stevenson, M.; Hung, D.V.; Hoang, T.H.; Mai Anh, L.; Tu Nguyen, T.H.; Le Tran, N. Evaluation of the Vietnamese A6 Mortality Reporting System: All-Cause Mortality. *Asia Pac. J. Public Health* **2015**, *27*, 733–742.
32. The National Oceanic and Atmospheric Administration's National Climate Data Center. Global Summary of the Day. 2015. Available online: http://www.ncdc.noaa.gov/ (accessed on 1 January 2015).
33. Tong, S.; FitzGerald, G.; Wang, X.Y.; Aitken, P.; Tippett, V.; Chen, D.; Wang, X.; Guo, Y. Exploration of the health risk-based definition for heatwave: A. multi-city study. *Environ. Res*. **2015**, *142*, 696–702.

34. Gasparrini, A.; Armstrong, B: The impact of heat waves on mortality. *Epidemiology* **2011**, *22*, 68–73.
35. Xu, Z.; Cheng, J.; Hu, W.; Tong, S. Heatwave and health events: A systematic evaluation of different temperature indicators, heatwave intensities and durations. *Sci. Total Environ.* **2018**, *630*, 679–689.
36. Lin, Y.K.; Ho, T.J.; Wang, Y.C. Mortality risk associated with temperature and prolonged temperature extremes in elderly populations in Taiwan. *Environ. Res.* **2011**, *111*, 1156–1163.
37. Zeng, W.; Lao, X.; Rutherford, S.; Xu, Y.; Xu, X.; Lin, H.; Liu, T.; Luo, Y.; Xiao, J.; Hu, M.; et al. The effect of heat waves on mortality and effect modifiers in four communities of Guangdong Province, China. *Sci. Total Environ.* **2014**, *482*, 214–221.
38. Bhaskaran, K.; Gasparrini, A.; Hajat, S.; Smeeth, L.; Armstrong, B. Time series regression studies in environmental epidemiology. *Int. J. Epidemiol* **2013**, *42*, 1187–1195.
39. Gasparrini, A.; Armstrong, B.; Kenward, M.G. Distributed lag non-linear models. *Stat. Med.* **2010**, *29*, 2224–2234.
40. Gasparrini, A. Distributed lag linear and non-linear models in R.: The package dlnm. *J. Stat. Softw.* **2011**, *43*, 1–20.
41. Gasparrini, A.; Armstrong, B. Reducing and meta-analysing estimates from distributed lag non-linear models. *BMC Med. Res. Methodol.* **2013**, *13*, 1.
42. Guo, Y.; Gasparrini, A.; Armstrong, B.; Li, S.; Tawatsupa, B.; Tobias, A. Global variation in the effects of ambient temperature on mortality: A systematic evaluation. *Epidemiology* **2014**, *25*, 781–789.
43. Semenza, J.C.; McCullough, J.E.; Flanders, W.D.; McGeehin, M.A.; Lumpkin, J.R. Excess hospital admissions during the July 1995 heat wave in Chicago. *Am. J. Prev. Med.* **1999**, *16*, 269–277.
44. Kovats, R.S.; Hajat, S.; Wilkinson, P. Contrasting patterns of mortality and hospital admissions during hot weather and heat waves in Greater London, UK. *Occup. Environ. Med.* **2004**, *61*, 893–898.
45. Semenza, J.C.; Rubin, C.H.; Falter, K.H.; Selanikio, J.D.; Flanders, W.D.; Howe, H.L.; Wilhelm, J.L. Heat-related deaths during the July 1995 heat wave in Chicago. *N. Engl. J. Med.* **1996**, *335*, 84–90.
46. Bouchama, A.; Dehbi, M.; Mohamed, G.; Matthies, F.; Shoukri, M.; Menne, B. Prognostic factors in heat wave related deaths: A meta-analysis. *Arch. Intern. Med.* **2007**, *167*, 2170–2176.
47. Nitschke, M.; Tucker, G.R.; Bi, P. Morbidity and mortality during heatwaves in metropolitan Adelaide. *Med. J. Aust.* **2007**, *187*, 662–665.
48. Giegi, G.; Pistelli, F.; Sherrill, D.L.; Maio, S.; Baldacci, S.; Carrozzi, L. Definition, epidemiology and natural history of COPD. *Eur. Respir. J.* **2007**, *30*, 993–1013.
49. Sprung, C.L: Heat stroke: Modern appraoch to an accident disease. *Chest* **1980**, *77*, 461–462.

2.8 Spatial variation of heat-related morbidity: A hierarchical Bayesian analysis in multiple districts of the Mekong Delta Region

Dung Phung [1,*], Cordia Chu [2], Dang Ngoc Tran [3], Cunrui Huang [1,*]

[1] Department of Health Policy & Management, School of Public Health, Sun Yat-sen University, Guangzhou, China
[2] Centre for Environment and Population Health, Griffith University, Queensland, Australia
[3] Faculty of Public Health, University of Medicine and Pharmacy, Ho Chi Minh City, Viet Nam

* Correspondence: d.phung@griffith.edu.au (D. P.), huangcr@mail.sysu.edu.cn (C. H.).

Phung D, Chu C, Tran DN, Huang C. Spatial variation of heat-related morbidity: A hierarchical Bayesian analysis in multiple districts of the Mekong Delta Region. Science of The Total Environment 2018;637-638:1559-1565.

Abstract: This study examined spatial variability of heat-related morbidity in multiple districts of the Mekong Delta Region (MDR), Vietnam. It was conducted in 132 district/cities of the MDR. We used a series of hierarchical Bayesian models to examine the region-wide and district-specific association between temperatures and hospitalizations from 2010 to 2013. The potential effects of seasonality, long-term trends, day of the week and holidays were controlled in the models. We also examined the influences of socio-demographic factors on the temperature-hospitalization relationship. The results indicate that an increase of 5 °C in average temperature was associated with a 6.1% increase (95%CI: 5.9, 6.2) in region-wide hospital admissions. However, the district-level risks ranged from a 55.2% decrease (95% CI: -54, -56) to a 24.4% increase (24.3–24.6) in admissions per 5 °C increase in average temperature. This reflects the heterogeneous magnitudes of temperature-hospitalization risk across districts. The results also indicate that temperature-hospitalization risk increased by 1.3% (95%CI: 1.2–1.4), for each increase of 1000 persons/ km2 in population density, 2.1% (95%CI: 2.04–2.11) for each 1% increase in percent of females, and 2.7% (95%CI: 2.6–2.8) for each 1% increase in percent of pre-school students. In contrast, the temperature-related hospitalization risk decreased up to 6.8% (95%CI: -6.6– -6.9) for each 1% increase in rural population. Public health intervention measures for both short-term and long-term effects of heat-related health risk should be developed with consideration of the use of city/district scale for the factors rather than the province scale. The province scale of factors does not accurately represent the variability of health risk due to exposure to high temperatures.

Keywords: Heat-related morbidity; Spatial variation; The Mekong Delta region; Vietnam

Introduction

Extreme temperature events, which are more frequent and intense due to global warming induced by increasing anthropogenic greenhouse gas emissions[1], are significantly associated with negative health impacts on populations worldwide[2-5]. Previous studies have indicated that high temperature has resulted in a significantly elevated risk of both morbidity[5-8] and mortality[3, 4, 9], and the adverse health outcomes associated with high temperatures are in a wide range of communicable[10-13] and non-communicable diseases[8, 14-16]. The studies[17-19] also indicated that the projected increase in temperature would result in a significantly increased burden of heat-related health effects in the future. However, the local impacts varied considerably across the regions and sub-regions[18, 19] due to the variability of localized microclimates created by the complexities of the physical and built environment[20], socioeconomic development[21], and adaptation strategies[17]. For example, a spatial variation in at-risk individuals across a city may result in areas with higher population sensitivity to temperature than others[22, 23]. A non-uniform spatial pattern in heat-related health risk has provided strong theoretical support for studies of the relationship between temperatures and health effects[5]. Thus evidence-based adaptation strategies should be encouraged at specific geographical locations. Nevertheless, evidence on spatial variation of heat-related morbidity has rarely been explored in developing countries, where temperature profiles and capacity to cope with extreme weather events may result in unexpected patterns and severity of temperature-related health risks[24].

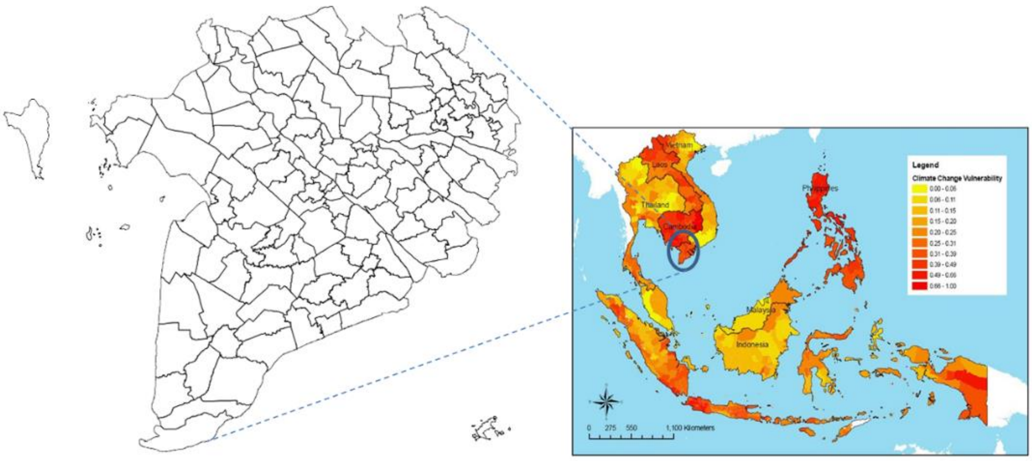
The Mekong Delta Region (MDR), which is a tropical region and includes the greatest number of provinces (13 provinces) in Vietnam, is considered one of the most vulnerable areas to climate risk in South- East Asia[25]. In a previous study, the mean temperature in the MDR was predicted to increase by up to 4 °C by the year 2100 and the number of days that have a mean temperature exceeding 35 °C will increase in the future[26]. Previous studies have indicated that temperature is one of the environmental determinants associated with elevated risk of diarrhoeal diseases[8, 12], dengue fever[27], hand foot and mouth disease[11], and paediatric hospitalizations for multiple causes[28]. A recent study conducted by Phung et al. [28] in several provinces of the MDR has indicated that a 1 °C increase in average temperature was associated with increased risk of 1.3% for all-causes, 2.2% for infectious, and 1.1% for respiratory diseases across the MDR. The study also found that socioeconomic factors such as population density, poverty rate, and illiteracy rate, and percentage of houses using safe water modified the temperature-hospitalization relationship[7]. However, these previous studies were conducted in either single-city or province-level areas which might not reflect actual spatial variation of socio-economic characteristics, physical and built environments of each research unit in the MDR. In Vietnam, province is the first and largest administrative level followed by the district level while the smallest administrative level is the commune. For example, population density and average income of a province are strongly influenced by its capital town or district but may not reflect conditions across that province.

In this study, we aimed to examine spatial variability in sensitivity to high temperature in several districts of the MDR, which are second-level administrative units in Vietnam, as well as the modification effects of socio-economic factors on heat-morbidity risk. Risk mapping at this geographical scale can help to identify vulnerable areas while better considering variation in population characteristics and other related factors. In addition, a district-level study can also support the development of more efficient strategies for resource allocation to mitigate the effects of climate change-related extreme weather events or adapt to them.

Methods

Research location

The Mekong Delta Region (MDR) is located in South-West Vietnam and has an area of 39,000 km2 with a population of 17.3 million people[29]. It has 13 provinces which comprise 131 districts and one capital city, Can Tho (Figure 1). The districts are classified in 4 types: city, town, urban and rural district depending on their socio-economic characteristics. The MDR has a tropical climate with two main seasons: the dry season (December–April) and the rainy season (May–November). Despite rapid urbanization, the population of the MDR relies on aquaculture and agriculture which are considered as the most productive in Vietnam. Since this is a coastal region located a little above sea level, the MDR is very sensitive to changes in hydrometeorological factors such as high temperatures and sea level rise and floods due to heavy precipitation events[25].



Source: Yusuf & Francisco, 2009

Figure. 1. A map of boundaries of the 132 districts in the Mekong Delta Region.

Data collection

We collected morbidity data from the daily hospital admissions for residents of each of 132 second-administrative units (hereafter is called districts) across the MDR. The admissions for external causes, comprising transport accidents, international self-harm, assault, medical complications, legal interventions, and hospital-related adverse events (ICD-10 Codes: V00-V99, X60-X84, X85-Y09, Y35-Y36, Y40-Y84, Y85-Y87.19, Y88-Y89.19) were excluded from the data analysis. Data were obtained from the daily admission records of 13 provincial/city hospitals for the January 2010-December 2013 period. Variables extracted from the admission records included primary and discharge diagnoses, dates of admission and discharge, age, sex, and address for each patient. Patients who were transferred from the outside of the MDR and a non-residential address did not meet the inclusion criteria.

Daily weather data were obtained from the 12 provincial hydro-meteorological stations from the January 2010 to December 2013. The data consists of daily minimum, maximum, and average temperatures (°C) and relative humidity (%), and daily cumulative rainfall (mm). Socio-demographic data at district level were obtained from the annual report of the provincial statistic office of each province. The available indicators, which could be considered as exploratory variables, comprised population, population density, % of population recorded by gender, % of pre-school students and % of rural population.

Data analysis

We used the hierarchical Bayesian models to examine the MDR-wide and district-specific association between temperatures and morbidity as well as the potential modification effects of socio-demographic factors on the temperature-morbidity relationship. We referred to the methods applied in the study by Hondula and Barnett[5]. Three steps involved in the data analysis. Firstly, we used a Poisson regression model in a Bayesian framework to estimate the MDR-wide effect of increased temperatures. The previous study[7] indicated that the hospitalizations were significantly associated with temperature on the same day (lag 0), so this study used the lag-0 day average temperature to relate the MDR-wide admissions. We explored the correlation between hospital admissions and maximum, minimum and average temperatures and found the highest correlation was with average temperature (ta). The regression model was following

$$Y_j \sim Poisson(\mu_j)$$

$$\text{Log}(\mu_j) = \alpha + \log(\text{E}) + time_j + temperature_j$$

$$time_j = hols_j + dow_j + doy_j$$

$$temperature_j = \beta * ta_j$$

where Yj is the observed number of hospital admissions on day j; E is an offset to control for population size across the MDR, and α is the intercept. The time component comprises categorical variables to account for holidays (*hols*) including all public holidays, day of week (*dow*) and day of year (*doy*) used to control for seasonality and long-term trends which are assumed to be unrelated to the short-term relationship between weather factors and admissions. We created natural cubic spline functions of the *doy* variable with five knots per year and four knots for the whole study period[30]. β is a linear coefficient that is the value change in hospital admissions associated with 5 °C increase in average temperature.

In the second step, we estimated the change in hospital admission associated with an increase in average temperature for each district/city while taking into account the spatial variability in admissions. The model is the following:

$$Y_{jk} \sim Poisson(\mu_{jk})$$

$$\text{Log}(\mu_{jk}) = \alpha + \log(\text{E}_k) + time_j + temperature_{jk} + \pi_k + smooth.area_k$$

$$time_j = hols_j + dow_j + doy_j$$

$$temperature_{jk} = \beta_k * ta_j$$

$$smooth.area_k = s(ew_k) + s(ns_k)$$

where *Yjk* is the observed number of hospital admissions at district k on day *j*; *Ek* is an offset to control for population size of district k; βk is the value change in hospital admissions associated with 5 °C increase in maximum temperature at district k. In this model we created the spatial smoother which comprised two spline functions (s) of geographical coordinate values with 2 degrees of freedom for the east-west (*ewk*) and north-south (*nsk*) to allow for the possibility of smooth but nonlinear change in risk across the region. *Ek* is the offset of population size of each district k. The heterogeneity which may comprise unusually high or low rates of admissions was controlled by a random intercept πk. All other variables and subscript definitions are described in the text following Model 1. The *βk* was modelled as a random effect for each district. The districts had significant positive temperature effect if the *βk* is positive and 95% credible interval (CI) excluding zero, whereas the districts have significant negative temperature effect if *βk* is negative and 95% credible interval (CI) excluding zero. Most of previous studies revealed the short-term relationship between temperatures and morbidity and mortality[2, 4, 9, 12], so this study examined the daily temperature-hospitalization relationship.

In the third step, we examined the influences of available socio-demographic factors on the spatial variability of temperature-admission relationship. In Model 3, we added a linear term Δ to modify the temperature slope (*βk*) using variables at the level of district. Model 3 is the following:

$$Y_{jk} \sim Poisson(\mu_{jk})$$

$$\text{Log}(\mu_{jk}) = \alpha + \log(\text{E}_k) + time_j + temperature_{jk} + \pi_k + smooth.area_k$$

$$time_j = hols_j + dow_j + doy_j$$

$$temperature_{jk} = \beta_k * ta_j$$

$$\beta_k = \beta^* + \Delta * dist.var_k$$

$$smooth.area_k = s(ew_k) + s(ns_k)$$

where β is the average temperature coefficient across all districts and *dist. vark* is the di is the district-level variables, comprising: district level (from urban to rural: 1 to 3), population density (×1000 persons/km2), female population (%), and percent of preschool student (%). The significant modification effect of a factor was revealed if the value of Δ was identified with 95%CI was excluded from zero. We first examined each dist. var factor using single-variable regression models with the input of a single independent variable, and then the models for multiple-variable regression model was developed with statistically significant variables identified from the single-variable regression models at the level of equal or less than 0.05. We used 5 °C increase in temperature, which is consistent with the difference in temperature between relatively hot and relatively cool summer days, to examine the association between temperature and hospital admission.

In summary, the parameters of interest computed by the models were β, the overall estimate of the temperature-admission risk; βk, the estimated temperature effect in each district k; and Δ, the estimated effect of each socio-demographic factor on temperature-admission risk. We reported associations between hospital admissions and a 5 °C increase in temperature from the minimum value of average temperature because the effects may be too small to present in some districts[5]. We used a burn-in and sample size of 10,000 Markov chain Monte Carlo (MCMC) simulations for the models. Non-informative N(0,1000) priors were used for all means and Gamma(1,1) priors for variances . We used the package "Bayesmh" developed for Stata software version 14.0 to examine temperature-admission effect using the Bayesian framework.

Results

The total number of hospital admissions from the 130 districts of the MDR throughout 2010–2013 was 2,061,001 cases, but two districts did not have any available data. The daily variation of admissions across the MDR (Figure 2) reflected the strong seasonal effect of admission which was higher in the wet season (May to November) than the dry season (December to April). The daily admissions of each district ranged from 0 to 178 cases with a mean of 11 cases per day. The daily average temperature across the MDR range ranged from 22.8 °C to 31.4 °C with a mean of 27.5 °C. In terms of socio-demographic factors, the population density of each district varied from 70 to 9000 persons/km2 with a mean of 700 persons/km2, and the distribution of the rural population was from 0 to 100% with a mean of 75%. The percentage distribution of female population ranged from 47% to 62% with a mean of 50% while preschool children ranged from 4 to 4536 with a mean of 2613 per 10,000 people.

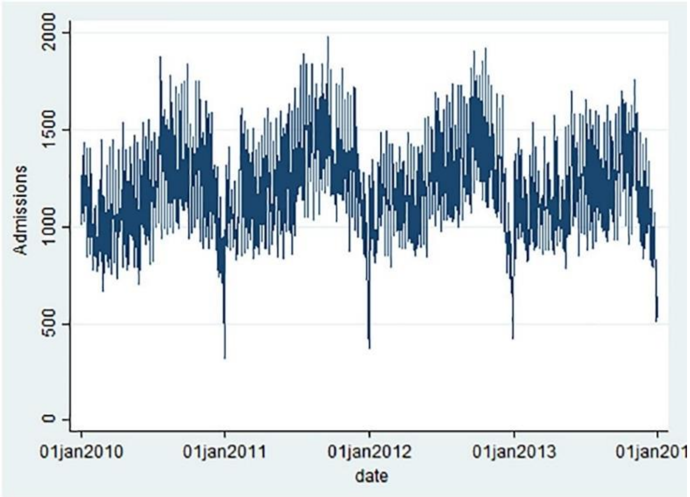


Figure. 2. Hospital admissions across the Mekong Delta Region

The result of the first model indicated that an increase of 5 °C in average temperature was associated with a statistically significant 6.1% increase (95%CI: 5.9, 6.2) in total hospital admissions across districts. This increase corresponds to 90 additional admissions per day relative to the average number of 1140 cases across the MDR. The second model, which was used to examine the association between temperature and hospital admissions at the district level, revealed that significant variability of the magnitudes of temperature-admission risk across 130 districts. The district-level risks ranged from 55.2% decrease (95%CI: -54, -56) to 24.4% (24.3–24.6) increase in admissions per 5 °C increase in average temperature. Statistically significant positive increases in temperature- admission risk at a rate of ≥10% were found in 43 districts, and a statistically significant decrease rate of ≥10% were found in 16 districts. Districts with the strongest positive associations between temperature and hospitalization were likely to be located along a north-to-south direction through the central city of the MDR. These districts tended to be located inland and along two large rivers, the Tien and Hau River; whereas, the districts with strong negative association tended to be located in South-West coastal areas and islands (Figure 3).

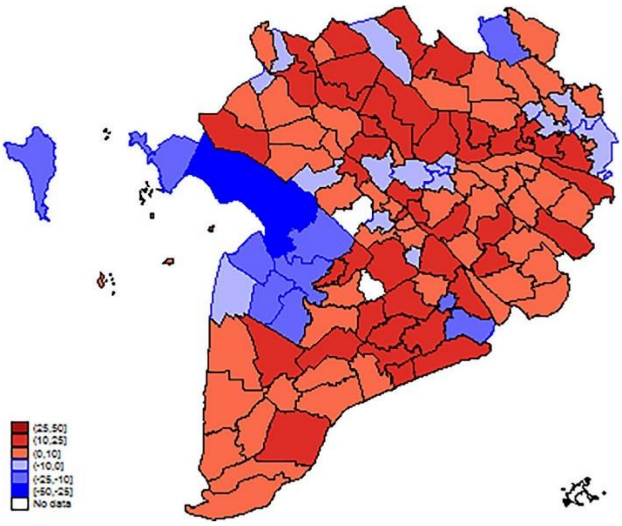


Figure. 3. The estimated association between temperature and hospital admission for each district in the MDR in term of the change in daily admissions percentage per 5 °C increase in temperature on the same day.

The results from Model 3, which examined the spatial pattern of temperature-related hospitalization risk in relation to sociodemographic factors, are presented in Table 1. Due to the availability of the data, this research involved only four factors, comprising: population density, % female and % of rural population, and % of preschool students. This data was complete for each district and believed to be associated with temperature-related risk. The models, which comprised a single variable, indicated that temperature-related hospitalization risk increased by 1.3% (95%CI: 1.2–1.4), 2.1% (95%CI: 2.04–2.11), and 2.7% (95%CI: 2.6–2.8). This indicates a statistically significant increase corresponding to of 1000 persons/km2 in population density and 1% in per- cent of female and pre-school students. However, the temperature-related hospitalization risk decreased by 0.1% (95%CI: -0.99–0.11) which correspond to a non-significant 1% increase in rural population. It is noteworthy that the temperature-related hospitalization risk decreased up to 6.8% (95%CI: -6.6– -6.8) when the population density was controlled in the multiple models. This demonstrated that there is the possibility of a negative interaction between population density and rural population. The influences of female and pre-school students on temperature-related hospitalization risks were not changed or changed to a small extent when the other factors were controlled in the multiple models (Table 1).

Table 1 Estimated % change in the temperature-hospitalization risk per unit change in district- level socio-demographic factors.

Variable	Unit change in predictor	Percent change in temperature-admissions slope (95%CI)
Single variable model		
Population density (persons/km^2)	1000	1.3 (1.2–1.4)
% of rural population	1	−0.1 (−0.99–(−0.11))
% of female population	1	2.1 (2.04–2.11)
% of pre-school students	1	2.7 (2.6–2.8)
Multiple variable model		
Population density (persons/km^2)	1000	−0.5 (−0.6–0.51)
% of rural population	1	−6.8 (−6.6–(−6.89))
% of female population	1	2.1 (2.09–2.11)
% of pre-school students	1	3.1 (3.08–3.11)

Discussion

This is the first study using the Bayesian framework to investigate the relationship between temperature and risk of hospitalization at a small geographical scale, specifically the district level in the Mekong Delta Region (MDR) in Vietnam. Overall, the results of this study reveal that higher temperatures were associated with a higher risk of daily hospitalization in the entire MDR. However, the association between temperature and hospitalizations is spatially heterogeneous with some of the districts having significant positive associations while others had negative associations. The population density, % of the female population and preschool students contributed to increasing temperature-hospitalization risk whereas the % of the rural population had a negative relationship with the temperature-hospitalization risk.

The findings of this study are consistent with that found from the previous studies [7]. This study has indicated that the risk of hospitalization increased 6% for every 5 °C increase in ambient temperatures on the same day in the MDR. This outcome is similar to the study by Phung et al. [7] which demonstrated an increase of 1.3% in hospitalization associated with every 1 °C increased in ambient temperatures on the same day in the MDR. This previous study also demonstrated that among hospitalizations, infectious and respiratory diseases were mostly associated with the high temperatures however this relationship was inconsistent with admissions due to cardiovascular diseases. The previous studies [31-34] provided strong evidence on the relationship between high temperatures and infectious diseases comprising food-, water-, and vector-borne diseases such as gastrointestinal infection, diarrhoea, and dengue fever. Similar evidence on the strong positive relationship between high temperatures and these infectious diseases were also presented by a series of studies conducted in the MDR [7, 12, 24, 27, 28, 35]. Some plausible mechanisms can be considered to explain the high temperature-infectious risk. Temperatures directly influence the replication and survival of bacteria which cause gastrointestinal infections. For example, Rotavirus and some of the diarrhoeal bacteria more rapidly proliferate in warm marine waters [36]. Likewise, high temperatures lead to rapid growth of bacteria, which cause food poisoning, in foods during the hot weather [37]. Variations in climatic factors can influence on the Aedes mosquitoes through multiple mechanisms since temperature is an important factor influencing biting rate, egg and immature mosquito development, the development time of virus in the mosquito, and survival at all stages of the mosquito life cycle [38]. For example, feeding behaviour is more frequent at higher temperatures, further affecting transmission risk. Finally, the dietary patterns and hygiene behaviour might be changed due to the change in temperatures. For example, storage of rainwater using inappropriate practices can result in mosquito-borne disease outbreaks, or high temperatures lead to higher consumption of water and reduced cooked foods which result in facilitating transmission of bacteria (Yang, 2017).

Similarly, the positive association between hot weather and elevated risk of hospital admissions due to respiratory diseases was revealed in previous independent studies [6, 39-41]. For instance, Turner et al. illustrated that 1 °C increase in temperature on hot days was associated with a 3.2% increase in respiratory morbidity [42]. The possible explanation for the relationship between heat and respiratory risk is related to the exacerbation of chronic obstructive pulmonary disease (COPD) is facilitated by exposure to heat. COPD is the most common cause of respiratory admissions among the elderly. Also, elderly with COPD have a higher risk of developing pulmonary vascular resistance secondary to peripheral pooling of blood or hypovolemia due to their inability to dissipate excess heat through circulatory adjustment. The elderly are revealed to be more sensitive to heat-related morbidity and mortality due to their diminished ability to thermos-regulate, increasing medical co-morbidities or use of medications, and social factors which may limit behavioural adaptation to increased temperatures [43]. The patients with conditions of co-morbidity such as neurological and psychiatric diagnoses (e.g. dementia) and using prescribed medication, especially for antipsychotics, antidepressants and hypnotics have been shown to increase in the risk of hospitalization and mortality [19, 44]. Plausible mechanisms underlying this include decreased thirst and decreased sweating [45]. The evidence from previous studies indicated that co-morbidity with cardiovascular, respiratory, renal disease and diabetes make patients more vulnerable to the effects of heat [46, 47].

The districts, which had significant adverse effects from high temperatures were mostly located in Kien Giang province which is coastal areas and islands in the Western MDR. The district, Hon Dat, with the strongest negative association, has the lowest population density (168 people/km2) and ample green space and open water to the sea so that these environmental factors could be related to the protective effect [5]. The spatial variation of hospitalization risks to high temperatures by districts within the MDR adds to a growing literature reporting the non-uniform effects within large metropolitan areas [5, 22, 48].

The previous studies indicated that the differences in sensitivity to heat would play an important role in developing and adopting mitigation strategies to cope with heat-related health risks in terms of city-specific heat thresholds, plans, and heat-related warning systems [49]. The study by Hondula and Barnett (2014) suggested that there were boundaries of isolated, vulnerable communities with higher sensitivity to heat-related health risk in their study in several areas in Brisbane. This finding reinforces a growing body of research supporting the need to consider within the city area the differences in sensitivity to heat when developing and conducting municipal emergency response measures and long-term action plans[5]. On the other hand, the attenuated temperature-health risk in rural areas might be caused by under-reporting of hospitalizations due to less opportunity to access to hospitals in some rurally remote and poor areas. This factor needs to be further studied in the future.

In this study, we also examined the influence of some sociodemographic factors on the spatial pattern of the relationship between high temperatures and risk of hospitalizations. The significant positive association between population density but the negative association between % of rural population reflect reflected the potential urban heat island effect which may occur in high building density cities and towns because of thermal properties of the built environment [5]. The two other factors, % of the female population and % of preschool students, were found to cause significant modification to temperature-hospitalization risk. This finding provides convincing evidence that females and children are highly vulnerable groups to heat-related health risk. The study by Phung et al. has indicated that 1 °C increase in temperatures was associated with 2.6%, 4.4%, and 3.8% increase in the risk of hospital admission due to all-cause, gastrointestinal and respiratory diseases among children aged 0–5 year-olds in the MDR[28]. Another study conducted in the multiple provinces of the MDR [7] suggested that females had higher sensitivity to heat-related risk of infectious and respiratory diseases than males. However, this finding was inconsistent with all-cause and other cause-specific diseases (e.g. cardiovascular diseases).

This study has several limitations. First, data on hospital admissions were collected from the provincial hospitals which admitted severe cases at a higher level for curative treatment. Thus minor cases which had minor health issues were admitted at the lower level hospitals (i.e. district hospitals) or private hospitals and might not be accounted for in this study. Second, the sample size is also a notable limitation in this study. Only 4 years of data were available for hospital admissions among residences within the research areas. Changes in area-level factors such as some socio-demographic characteristics may not occur in a short period, so longer time-span data sets based on more years might provide better support for evaluation of area-level variability in sensitivity and area-level factors related to heterogeneous heat-related health risk. Third, because of the downscale classification of areas from provinces to districts, the number of cases for cause-specific diseases was not sufficient for examining the short-term temperature health effects in each district. Therefore, this study was unable to examine the effect of temperature on a specific disease or groups of diseases but only the all-cause hospitalizations. Fourth, there was a lack of some meteorological factors such as air pressure and wind speed although some recent studies have indicated that these factors were positively associated with risk of diseases, especially infectious diseases [50, 51]. Finally, as ecological study design, this study had no access to individual-level data such as information on adaptive measures (e.g. air conditioning), occupation, or outdoor/dynamic indoor activities which may reflect the actual exposure to temperatures of each. It is difficult to deal with this limitation due to complication monitoring of temperature exposures for each however the future study may use a hybrid study design which incorporates individual-level data of a sub-population to improve ecological inference. This study design is described elsewhere [52-54].

Conclusions

The results of this multiple-area study at the district scale reinforce the evidence that high temperatures are associated with statistically significant levels of elevated risk of hospital admissions in the Mekong Delta region. However, the spatial patterns of temperature-hospitalization risk relationship vary across the districts which are the second scale of geographical and administrative management unit used in Vietnam. Thus our findings reflect two important implications. First, the Mekong Delta Region (MDR) is highly vulnerable to climate change, and temperatures in this region have been predicted to increase in the future continuously. This implies that the projected morbidity and mortality associated with high temperatures will increase in the future due to climate change phenomenon if there is no appropriate interventional strategy. Second, the adaptation and intervention measures for both short-term and long-term effects of heat-related health risk should be developed with the consideration of the city/district scale rather than the provincial scale. The provincial level does not comprehensively evaluate the variability of health risk due to exposure to high temperatures. The public health intervention programs such as improving the capacity of the health sector in climate change adaptation, educating community members in minimizing the effects of high temperature, developing temperature-health risk early warning systems, establishing temperature shelters in residential hot spots, etc. should be implemented. These measures may help to cope with the additional burden of disease and help to protect residents from changing temperature conditions related to climate change.

References

1. IPCC, W. G. I., Climate change 2007: the physical science basis contribution of working group I. Fourth assessment report of the intergovernmental panel on climate change. Cambridge University Press, Cambridge **2007**.
2. Gasparrini, A.; Guo, Y.; Hashizume, M.; Kinney, P. L.; Petkova, E. P.; Lavigne, E.; Zanobetti, A.; Schwartz, J. D.; Tobias, A.; Leone, M., Temporal variation in heat–mortality associations: a multicountry study. *Environ Health Persp* **2015**, 123, (11), 1200-1207.
3. Gasparrini, A.; Guo, Y.; Hashizume, M.; Lavigne, E.; Zanobetti, A.; Schwartz, J.; Tobias, A.; Tong, S.; Rocklöv, J.; Forsberg, B., Mortality risk attributable to high and low ambient temperature: a multicountry observational study. *The Lancet* **2015**, 386, (9991), 369-375.
4. Guo, Y.; Gasparrini, A.; Armstrong, B.; Li, S.; Tawatsupa, B.; Tobias, A.; Lavigne, E.; Coelho, M. d. S. Z. S.; Leone, M.; Pan, X., Global variation in the effects of ambient temperature on mortality: a systematic evaluation. *Epidemiology* (Cambridge, Mass.) **2014**, 25, (6), 781.
5. Hondula, D. M.; Barnett, A. G., Heat-related morbidity in Brisbane, Australia: spatial variation and area-level predictors. *Environ Health Persp* **2014**, 122, (8), 831-836.
6. Michelozzi, P.; Accetta, G.; De Sario, M.; D'Ippoliti, D.; Marino, C.; Baccini, M.; Biggeri, A.; Anderson, H. R.; Katsouyanni, K.; Ballester, F., High temperature and hospitalizations for cardiovascular and respiratory causes in 12 European cities. *American journal of respiratory and critical care medicine* **2009**, 179, (5), 383-389.
7. Phung, D.; Guo, Y.; Nguyen, H. T. L.; Rutherford, S.; Baum, S.; Chu, C., High temperature and risk of hospitalizations, and effect modifying potential of socio-economic conditions: A multi-province study in the tropical Mekong Delta Region. *Environment international* **2016**, 92, 77-86.
8. Phung, D.; Huang, C.; Rutherford, S.; Chu, C.; Wang, X.; Nguyen, M.; Nguyen, N. H.; Do, C. M.; Nguyen, T. H., Temporal and spatial patterns of diarrhoea in the Mekong Delta area, Vietnam. *Epidemiology & Infection* **2015**, 143, (16), 3488-3497.
9. Huang, C.; Barnett, A. G.; Wang, X.; Tong, S., Effects of extreme temperatures on years of life lost for cardiovascular deaths: a time series study in Brisbane, Australia. *Circulation: Cardiovascular Quality and Outcomes* **2012**, 5, (5), 609-614.
10. Milazzo, A.; Giles, L. C.; Zhang, Y.; Koehler, A. P.; Hiller, J. E.; Bi, P., The effect of temperature on different Salmonella serotypes during warm seasons in a Mediterranean climate city, Adelaide, Australia. *Epidemiology & Infection* **2016**, 144, (6), 1231-1240.
11. Nguyen, H. X.; Chu, C.; Nguyen, H. L. T.; Nguyen, H. T.; Do, C. M.; Rutherford, S.; Phung, D., Temporal and spatial analysis of hand, foot, and mouth disease in relation to climate factors: a study in the Mekong Delta region, Vietnam. *Science of the Total Environment* **2017**, 581, 766-772.
12. Phung, D.; Huang, C.; Rutherford, S.; Chu, C.; Wang, X.; Nguyen, M.; Nguyen, N. H.; Do Manh, C.; Nguyen, T. H., Association between climate factors and diarrhoea in a Mekong Delta area. *International journal of biometeorology* **2015**, 59, (9), 1321-1331.
13. Xiang, J.; Hansen, A.; Liu, Q.; Liu, X.; Tong, M. X.; Sun, Y.; Cameron, S.; Hanson-Easey, S.; Han, G.-S.; Williams, C., Association between dengue fever incidence and meteorological factors in Guangzhou, China, 2005–2014. *Environmental research* **2017**, 153, 17-26.
14. Bayentin, L.; El Adlouni, S.; Ouarda, T. B. M. J.; Gosselin, P.; Doyon, B.; Chebana, F., Spatial variability of climate effects on ischemic heart disease hospitalization rates for the period 1989-2006 in Quebec, Canada. *International journal of health geographics* **2010**, 9, (1), 5.
15. Ebi, K. L.; Exuzides, K. A.; Lau, E.; Kelsh, M.; Barnston, A., Weather changes associated with hospitalizations for cardiovascular diseases and stroke in California, 1983–1998. *International journal of biometeorology* **2004**, 49, (1), 48-58.

16. Turner, L. R.; Barnett, A. G.; Connell, D.; Tonga, S., Ambient temperature and cardiorespiratory morbidity: a systematic review and meta-analysis. *Epidemiology* **2012**, 594-606.
17. Huang, C.; Barnett, A. G.; Wang, X.; Vaneckova, P.; FitzGerald, G.; Tong, S., Projecting future heat-related mortality under climate change scenarios: a systematic review. *Environ Health Persp* **2011**, 119, (12), 1681-1690.
18. Knowlton, K.; Lynn, B.; Goldberg, R. A.; Rosenzweig, C.; Hogrefe, C.; Rosenthal, J. K.; Kinney, P. L., Projecting heat-related mortality impacts under a changing climate in the New York City region. *American journal of public health* **2007**, 97, (11), 2028-2034.
19. Page, L. A.; Hajat, S.; Kovats, R. S.; Howard, L. M., Temperature-related deaths in people with psychosis, dementia and substance misuse. *The British Journal of Psychiatry* **2012**, 200, (6), 485-490.
20. Bassil, K. L.; Cole, D. C.; Moineddin, R.; Craig, A. M.; Lou, W. Y. W.; Schwartz, B.; Rea, E., Temporal and spatial variation of heat-related illness using 911 medical dispatch data. *Environmental research* **2009**, 109, (5), 600-606.
21. Rey, G.; Fouillet, A.; Bessemoulin, P.; Frayssinet, P.; Dufour, A.; Jougla, E.; Hémon, D., Heat exposure and socio-economic vulnerability as synergistic factors in heat-wave-related mortality. *European journal of epidemiology* **2009**, 24, (9), 495-502.
22. Hondula, D. M.; Davis, R. E.; Leisten, M. J.; Saha, M. V.; Veazey, L. M.; Wegner, C. R., Fine-scale spatial variability of heat-related mortality in Philadelphia County, USA, from 1983-2008: a case-series analysis. *Environ Health-Glob* **2012**, 11, (1), 16.
23. Reid, C. E.; O'neill, M. S.; Gronlund, C. J.; Brines, S. J.; Brown, D. G.; Diez-Roux, A. V.; Schwartz, J., Mapping community determinants of heat vulnerability. *Environ Health Persp* **2009**, 117, (11), 1730-1736.
24. Phung, D.; Chu, C.; Rutherford, S.; Nguyen, H. L. T.; Do, C. M.; Huang, C., Heatwave and risk of hospitalization: A multi-province study in Vietnam. *Environ Pollut* **2017**, 220, 597-607.
25. Yusuf, A. A.; Francisco, H., Climate change vulnerability mapping for Southeast Asia. **2009**.
26. Chaudhry, P.; Ruysschaert, G., Climate Change and human development in Vietnam. UNDP Human Development Report Office. Occasional paper **2008**.
27. Phung, D.; Huang, C.; Rutherford, S.; Chu, C.; Wang, X.; Nguyen, M.; Nguyen, N. H.; Do Manh, C., Identification of the prediction model for dengue incidence in Can Tho city, a Mekong Delta area in Vietnam. *Acta tropica* **2015**, 141, 88-96.
28. Phung, D.; Rutherford, S.; Chu, C.; Wang, X.; Nguyen, M.; Nguyen, N. H.; Do, C. M.; Nguyen, T. H.; Huang, C., Temperature as a risk factor for hospitalisations among young children in the Mekong Delta area, Vietnam. *Occup Environ Med* **2015**, 72, (7), 529-535.
29. Gso, Statistical yearbook of Vietnam. In General Statistics Office of Vietnam Hanoi: **2011**.
30. Gasparrini, A.; Armstrong, B.; Kenward, M. G., Distributed lag non-linear models. *Statistics in medicine* **2010**, 29, (21), 2224-2234.
31. Allard, R.; Plante, C.; Garnier, C.; Kosatsky, T., The reported incidence of campylobacteriosis modelled as a function of earlier temperatures and numbers of cases, Montreal, Canada, 1990–2006. *International journal of biometeorology* **2011**, 55, (3), 353-360.
32. Harper, S. L.; Edge, V. L.; Schuster-Wallace, C. J.; Berke, O.; McEwen, S. A., Weather, water quality and infectious gastrointestinal illness in two Inuit communities in Nunatsiavut, Canada: potential implications for climate change. *EcoHealth* **2011**, 8, (1), 93-108.
33. Lal, A.; Hales, S.; Kirk, M.; Baker, M. G.; French, N. P., Spatial and temporal variation in the association between temperature and salmonellosis in NZ. *Australian and New Zealand journal of public health* **2016**, 40, (2), 165-169.
34. Wang, L.-x.; Li, X.-j.; Fang, L.-q.; Wang, D.-c.; Cao, W.-c.; Biao, K. A. N., Association between the incidence of typhoid and paratyphoid fever and meteorological variables in Guizhou, China. *Chinese medical journal* **2012**, 125, (3), 455-460.

35. Phung, D.; Talukder, M. R. R.; Rutherford, S.; Chu, C., A climate-based prediction model in the high-risk clusters of the Mekong Delta region, Vietnam: towards improving dengue prevention and control. *Tropical Medicine & International Health* **2016**, 21, (10), 1324-1333.
36. Moe, K.; Shirley, J. A., The effects of relative humidity and temperature on the survival of human rotavirus in faeces. *Archives of virology* **1982**, 72, (3), 179-186.
37. Bentham, G.; Langford, I. H., Environmental temperatures and the incidence of food poisoning in England and Wales. *International journal of biometeorology* **2001**, 45, (1), 22-26.
38. Ebi, K. L.; Nealon, J., Dengue in a changing climate. *Environmental research* **2016**, 151, 115-123.
39. Green, R. S.; Basu, R.; Malig, B.; Broadwin, R.; Kim, J. J.; Ostro, B., The effect of temperature on hospital admissions in nine California counties. *International Journal of Public Health* **2010**, 55, (2), 113-121.
40. Linares, C.; Diaz, J., Impact of high temperatures on hospital admissions: comparative analysis with previous studies about mortality (Madrid). *European Journal of Public Health* **2007**, 18, (3), 317-322.
41. Wichmann, J.; Andersen, Z.; Ketzel, M.; Ellermann, T.; Loft, S., Apparent temperature and cause-specific emergency hospital admissions in Greater Copenhagen, Denmark. *PLoS One* **2011**, 6, (7), e22904.
42. Turner, L. R.; Connell, D.; Tong, S., Exposure to hot and cold temperatures and ambulance attendances in Brisbane, Australia: a time-series study. *BMJ open* **2012**, 2, (4), e001074.
43. Arbuthnott, K. G.; Hajat, S., The health effects of hotter summers and heat waves in the population of the United Kingdom: a review of the evidence. *Environ Health-Glob* **2017**, 16, (1), 119.
44. Sommet, A.; Durrieu, G.; Lapeyre-Mestre, M.; Montastruc, J. L.; Association of French PharmacoVigilance, C., A comparative study of adverse drug reactions during two heat waves that occurred in France in 2003 and 2006. *Pharmacoepidemiology and Drug Safety* **2012**, 21, (3), 285-288.
45. Stöllberger, C.; Lutz, W.; Finsterer, J., Heat-related side-effects of neurological and non-neurological medication may increase heatwave fatalities. *European journal of neurology* **2009**, 16, (7), 879-882.
46. Naughton, M. P.; Henderson, A.; Mirabelli, M. C.; Kaiser, R.; Wilhelm, J. L.; Kieszak, S. M.; Rubin, C. H.; McGeehin, M. A., Heat-related mortality during a 1999 heat wave in Chicago. *American journal of preventive medicine* **2002**, 22, (4), 221-227.
47. Schwartz, J., Who is sensitive to extremes of temperature?: A case-only analysis. *Epidemiology* **2005**, 16, (1), 67-72.
48. Vaneckova, P.; Beggs, P. J.; Jacobson, C. R., Spatial analysis of heat-related mortality among the elderly between 1993 and 2004 in Sydney, Australia. *Social science & medicine* **2010**, 70, (2), 293-304.
49. Sheridan, S. C.; Kalkstein, L. S., Progress in heat watch–warning system technology. *Bulletin of the American Meteorological Society* **2004**, 85, (12), 1931-1942.
50. Xu, C.; Li, Y.; Wang, J.; Xiao, G., Spatial-temporal detection of risk factors for bacillary dysentery in Beijing, Tianjin and Hebei, China. *BMC public health* **2017**, 17, (1), 743.
51. Xu, C.; Xiao, G.; Wang, J.; Zhang, X.; Liang, J., Spatiotemporal risk of bacillary dysentery and sensitivity to meteorological factors in Hunan province, China. *Int J Env Res Pub He* **2017**, 15, (1), 47.
52. Haneuse, S.; Bartell, S., Designs for the combination of group-and individual-level data. *Epidemiology* (Cambridge, Mass.) **2011**, 22, (3), 382.
53. Haneuse, S.; Wakefield, J., Geographic-based ecological correlation studies using supplemental case–control data. *Statistics in Medicine* **2008**, 27, (6), 864-887.

54. Jackson, C.; Best, N.; Richardson, S., Improving ecological inference using individual-level data. *Statistics in medicine* **2006**, 25, (12), 2136-2159.

2.9 Mortality burden attributable to heatwaves in Thailand: A systematic assessment incorporating evidence-based lag structure

Cunrui Huang [1,#], Jian Cheng [2,#], Dung Phung [1,3], Benjawan Tawatsupa [4], Wenbiao Hu [2,*], Zhiwei Xu [2,*]

[1] School of Public Health, Sun Yat-sen University, Guangzhou, China
[2] School of Public Health and Social Work, Queensland University of Technology, Brisbane, Australia
[3] Centre for Environment and Population Health, Griffith University, Brisbane, Australia
[4] Health Impact Assessment Division, Department of Health, Ministry of Public Heath, Bangkok, Thailand
[#] These authors contributed equally to this work.
[*] Correspondence: w2.hu@qut.edu.au (W. H.), xzw1011@gmail.com (Z. X.)

Huang C, Cheng J, Phung D, Tawatsupa B, Hu W, Xu Z. Mortality burden attributable to heatwaves in Thailand: A systematic assessment incorporating evidence-based lag structure. Environment International 2018;121:41-50.

Abstract:

Background: Available information on the acute and cumulative effects of heatwaves on cause-specific mortality in Thailand is scarce. Objective: To quantify the acute and cumulative effects of heatwaves on mortality in Thailand, and assess heatwave-related mortality burden.

Methods: Thirty heatwave definitions were used and categorized into three groups: low-intensity heatwaves (HW_{low}), middle intensity heatwaves (HW_{middle}), and high-intensity heatwaves (HW_{high}). Time-series analyses were conducted to examine the acute and cumulative effects of HW_{low}, HW_{middle}, and HW_{high} on total and cause-specific mortality in 60 provinces of Thailand, incorporating an optimal lag for each cause and each province. Random-effects meta-analyses were performed to pool provincial estimates to national estimates for both acute and cumulative effects. Meta-regressions were conducted to identify the possible factors contributing to the spatial heterogeneity of heatwave vulnerability.

Results: The cumulative effects of HW_{low} and HW_{middle} on total and cause-specific mortality were greater than HW_{high}. Both acute and cumulative effects of HW_{low}, HW_{middle} and HW_{high} on neoplasms and certain infectious and parasitic diseases were among the highest across all death causes. Effects of heatwaves on deaths from endocrine, nutritional and metabolic diseases appeared to be longer-lasting, and the effects of heatwaves on deaths from ischaemic heart diseases and pneumonia occurred more rapidly. Northern and Central Thailand were the regions vulnerable to heatwaves, and the proportion of the elderly population was the major driver behind the spatial heterogeneity of heatwave vulnerability.

Conclusions: More attention needs to be paid to mild heatwaves. Future heatwave-related mortality burden due to neoplasms and infectious diseases in Thailand may increase as climate change continues.

Keywords: Cause-specific mortality; Heatwave; Thailand

Introduction

Climate change has been considered as the biggest global health threat in the 21st century [1], and properly tackling its adverse impacts can be the greatest opportunity to improve public health [2]. Increasing global surface temperature is the most symbolic parameter of climate change [3] and high ambient temperature, especially prolonged extreme high temperature (i.e., heatwave) [4-6], has caused substantial health burden globally [7]. There is no universal consensus on how to well define heatwaves so far [8] and a slight change in heatwave definition may have a considerable impact on the estimated health effect [9]. A recent multi-country study which used four temperature thresholds to define heatwaves has observed that the association between heat waves and total mortality increased with increasing temperature thresholds [10]. To better facilitate the development of tailored and cost-effective heatwave-prevention strategies (e.g., heatwave early warning system), it is judicious to categorize heatwaves of various intensities into several groups while evaluating the health effects of heatwaves [8, 11].

The effect of heat waves on mortality appeared not just on the same day of exposure, but also lasted for a few days (i.e., lag effect) [10]. Further, mortality increase during heatwaves in some regions may be followed by a mortality decrease after heatwaves due to the decrease in the population of susceptible pool (i.e., harvesting effect) [12]. The widely-observed harvesting effects could, to some extent, affect or bias the assessment of the overall heatwave-related health burden [13]. It is possible that spatially variable population vulnerability to heatwaves due to different contexts, such as demographic characteristics [14] and adaptation capacities [15], results in the heterogeneity of heatwave effects across different regions, mainly in terms of lag structure and effect size. Also, the lag structure of health effects of different-intensity heatwaves on the same city may also be different as more intense heatwaves may trigger deaths more promptly and have a longer-lasting harvesting effect [10]. Therefore, it is desirable to scientifically consider evidence-based lag structure to accurately assess heatwave-related health burden. For example, Hertel et al. have used generalized cross-validation to determine the optimal lag period when looking at the heatwave effect on cause-specific mortality in Essen, Germany [16].

A population/community's heatwave vulnerability is mainly determined by three factors: exposure, sensitivity, and adaptive capacity. Thus, heatwave vulnerability varies considerably across different communities due to their various exposure levels, as well as different demographic and adaptation characteristics [10]. It is crucial to identify those communities/populations which are more vulnerable to heatwave impacts for wisely allocating limited health resources to help those who are most in need [17].

The heatwave definition of World Meteorological Organization is "when the daily maximum temperature of more than five consecutive days exceeds the maximum normal temperature by 5 °C, the "normal" period being defined as 1961-1990". This definition has been adopted by the Thai Meteorological Department, and thus Thailand has been considered as rarely experiencing heatwaves. However, heatwaves should not be assessed without reference to its human health impacts although it is generally considered as a meteorological event [18], and prior studies have observed considerable adverse effects of heat and heatwaves (using a few widely used definitions) on mortality in Thailand [10, 19]. However, to the best of our knowledge, no study has characterized the effects of heatwaves on cause-specific mortality in Thailand.

This study aimed to quantify the effects of heatwaves on total and cause-specific mortality in 60 provinces of Thailand, a country where the health effects of heatwaves have not been adequately evaluated. Specifically, this study attempted to answer four research questions: 1). How did different-intensity heatwaves affect total and cause-specific mortality in Thailand? 2). What were the total and cause-specific mortality burdens attributable to different-intensity heatwaves after incorporating evidence-based lag structure? 3). What was the spatial distribution of the heatwave effects on mortality in Thailand? 4). What were the possible factors contributing to the heterogeneity of heatwave effects across different provinces of Thailand?

Methods

Study site

Thailand is located in the tropical area, with latitudes ranging from 5° 37' N to 20° 27' N and longitudes ranging from 97° 22' E to 105° 37' E. Upper part of Thailand, e.g., Northern Thailand and Northeastern Thailand, usually experiences a long period of warm weather, and maximum temperatures can reach 40 °C or more. As a developing country, public health resources in Thailand, especially those used for preventing and controlling heat impact, are limited. The great exposure to heat and the relatively low adaptive capacity may make Thailand residents vulnerable to the adverse impact of heatwaves.

Data collection

Daily data on non-external cause-specific deaths (International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10): A00-R99) from 1st January 1999 to 31st December 2008 in 60 provinces of Thailand were obtained from Ministry of Public Health, Thailand. To specifically analyze the relationship between heatwaves and cause-specific deaths, we extracted the daily number of deaths due to the following diseases: certain infectious and parasitic diseases (A00-B99), neoplasms (C00-D48), malignant neoplasms (C00-97), endocrine, nutritional and metabolic diseases (E00-90), diabetes mellitus (E10-14), diseases of the circulatory system (I00-99), ischaemic heart diseases (I20-25), diseases of the respiratory system (J00-99), pneumonia (J12-18), diseases of the digestive system (K00-93), diseases of the genitourinary system (N00-99), and renal failure (N17-19). Daily climatic data for each province which covered the same period, including maximum temperature, minimum temperature, mean temperature and relative humidity, were provided by Meteorological Department, Ministry of Digital Economy and Society, Thailand.

Data on the possible factors contributing to the heterogeneity of heatwave effects on deaths across provinces (population heatwave sensitivity modifiers), including population density, average years of education attainment of population aged 15 years and over, proportion of people aged ≥60 years, proportion of people aged ≥65 years, proportion of people aged ≥70 years, proportion of people aged ≥75 years, and proportion of one-person households, were obtained from the results of Thailand 2000 Population and Housing Census [20]. There were three censuses in Thailand (year 1990, year 2000 and year 2010) from year 1990 until now, and we chose the information from year 2000 Census because our study period covered this year and also because this census results included the most relevant/thorough information on possible factors associated with heatwave effect. No information on gross provincial product per capita (GPPPC) (heatwave adaptive capacity modifier) was found in this census results, and thus we used the GPPPC in 2013 as a proxy [21]. We also used the average values of mean temperature as well as relative humidity in each province as the indicators for heatwave exposure level modifiers. The details of these factors were presented in Table S1 (supplementary material). Ethics approval was granted by the Ethics Committee of Sun Yat-sen University before the data collection.

Heatwave definitions

The four hottest months (March to June) from 1999 to 2008 were chosen as the study period in this study. Heatwave was defined by incorporating duration and intensity [8]. To comprehensively explore how different heatwaves affect mortality in Thailand, we adopted the most commonly used 10 intensities (90^{th}, 91^{st}, 92^{nd}, …, or 99^{th} percentile of the mean temperature across the study period) and three durations (i.e., ≥ 2, 3 or 4 consecutive days) in the existing literature to define a heatwave. Thus, we used a total of 30 heatwaves definitions. For the development of cost-effective heatwave early warning system, it is desirable to categorize heatwaves into different groups according to its intensity. Our prior work has observed that grouping heatwaves into three categories seemed reasonable [11], and Nairn has also proposed to group heatwaves into three categories [22, 23]. We categorized these 30 heatwave definitions into three groups: low-intensity heatwaves (HWlow), middle intensity heatwaves (HWmiddle), and high-intensity heatwaves (HWhigh). This classification may provide practical evidence to development of heatwave early warning system as policymakers can decide when to trigger the system based on heatwave intensity and it is easy for the public to understand the classification.

Statistical analysis

Three-stage analyses were conducted in this study. In the first stage, we quantified the effects of 30 different heatwaves on total and cause-specific deaths in each province (i.e., relative risk (RR)). In the second stage, in each province, we pooled the RRs of 30 heatwaves into three different intensity heatwave groups (i.e. HW_{low}, HW_{middle}, and HW_{high}), and also calculated the attributable fraction (AF) and attributable death numbers (AN) [24] under three different intensity heatwave groups accordingly [25]. Finally, we pooled RRs and summed ANs of all provinces and obtained national estimates of RRs and ANs for three different intensity heatwave groups. In the third stage, we used meta-regression to identify the possible factors contributing to the heterogeneity of heatwave effects across different provinces under HW_{low}, HW_{middle}, and HW_{high} using RR of each province as the outcome variable.

First-stage analysis

A quasi-Poisson generalized additive model was used to quantify the effects of heatwaves on total and cause-specific deaths in each province [26]. A natural cubic spline with three degrees of freedom (*df*) was used to control for the long-term trend and with-in season variation [27]. A categorical variable was used to control for day of the week [10]. Relative humidity was also controlled for in the model with linear function for the current day's value (lag 0) as our primary analyses showed that using spline function with different *dfs* and for different lag, days did not change the main results.

We conducted two different types of analyses using distributed non-linear lag model (DLNM) [28] to specifically quantify the acute effects of heatwaves and to assess the cumulative effects of heatwaves (considering the prolonged effect of heatwaves or harvesting effect) [29]. To capture the acute effects of heatwaves on deaths, we used a fixed lag for 0-1 days (i.e., the current day of exposure and the next day). To investigate the cumulative effects of heatwaves, we used generalized cross-validation (GCV) [16] to identify an optimal lag within a range of lag 1 day to lag 21 days [7], and then calculated the effect of each heatwave on deaths under the optimal lag. This approach to capturing the cumulative effects of heatwaves has been well used in our prior work [29].

Second-stage analysis

To pool the RRs of 30 heatwaves into three different intensity heatwave groups in each province, we used random-effects meta-analysis through maximum likelihood [30]. To pool RRs of all provinces together for a national estimate, we also used the same meta-analysis approach. The detailed equations for calculating the AF and AN were:

$$AF_{ij} = \frac{RR_{ij} - 1}{RR_{ij}}$$

$$AN_{ij} = AF_{ij} * \sum_{1}^{n} D_{ijn}$$

Where: AF_{ij} indicates the attributable fraction in region (i, range:1-60) under the heatwave definition (j, rang1-60); RR_{ij} is the estimated relative risk obtained from the first-stage analysis; AN_{ij} indicates the attributable number; $\sum_1^n D_{ijn}$ is the total deaths (D) summed over all identified heatwave episodes (n, range ≥1) in region (i) under the heatwave definition (j). The attributable fraction and attributable number for one heatwave category (low, medium or high) was computed with the averaged AF_{ij} and AN_{ij} across all heatwave definitions that conditions on the significant RR_{ij} above 1.0. In other words, when heatwave effects under a certain heatwave definition were not statistically significant, the AF and AN would be assumed to be zero. The national attributable number was calculated by summing up all regional specific estimates. This approach has been well utilized in our previous study [24].

Third-stage analysis

Potential factors contributing to the heterogeneity of heatwave effects across different provinces (Table S1) were assessed using random-effects meta-regression single predictor models [10, 24]. Residual heterogeneity was examined and then quantified by the Cochran Q test and I2 statistic.

All statistical analyses were conducted in R (version 3.4.0), and the visual mappings were done in ArcGIS (version 10.5). The packages "dlnm" and "metafor" were used to conduct distributed non-linear lag models and meta-regression analyses [30, 31].

Results

Summary statistics

Table 1 showed the details of these heatwave definitions and categories. Figure S1 (supplementary material) presented the values of mean temperature for each heatwave definition in each province and Thailand. The bold black line and points represent the mean temperatures averaged across 60 provinces of Thailand. Other lines and points in different colours represent the province-specific mean temperatures.

Table 2 presented the average values of climatic factors and cause-specific deaths of all provinces in the study period. The average value of mean temperature ranged from 25.07 °C in Chiang Rai to 29.26 °C in Bangkok. Neoplasms, certain infectious and parasitic diseases, and diseases of the circulatory systems were the three leading causes of deaths in Thailand in the study period, followed by diseases of the respiratory system

Acute effects of heatwaves on total and cause-specific deaths

Table 3 showed the pooled acute effects of HW_{low}, HW_{middle} and HW_{high} on total and cause-specific deaths in Thailand, suggesting that deaths from certain infectious and parasitic diseases, ischaemic heart diseases, and pneumonia were the three leading causes which were most sensitive to HW_{low}, HW_{middle} and HW_{high}. The acute effects of HW_{low} on deaths from diseases of the respiratory system and diseases of the circulatory system were not very high compared with deaths from other diseases. The acute effect of heatwaves on deaths from endocrine, nutritional and metabolic diseases was relatively high under HW_{low}, but was not high under HW_{middle} or HW_{high}.

Cumulative effects of heatwaves on total and cause-specific deaths

The pooled cumulative effects of HW_{low}, HW_{middle}, and HW_{high} on total and cause-specific deaths in Thailand, which were shown in Table 4, were higher than the acute effects in Table 3, indicating that heatwave effects in Thailand occurred beyond one to two days (Figure S2 (supplementary material)). Intriguingly, the pooled cumulative effects on total and cause-specific deaths decreased when heatwave intensity increased. Further, the ranks of cause-specific deaths also changed in Table 4 compared with Table 3. Deaths from certain infectious and parasitic diseases were still the leading cause of deaths which was most sensitive to HW_{low}, HW_{middle}, and HW_{high}, but the cumulative effects of HW_{low} and HW_{middle} on diabetes mellitus ranked very high, compared with the acute effects. Comparing the ranks of cause-specific deaths across HW_{low}, HW_{middle}, and HW_{high} in Table 4, we observed that the ranks of cause-specific deaths sensitive to HW_{low} and HW_{middle} were similar, but it changed substantially under HW_{high}.

Number of deaths attributable to heatwaves

Table 5 showed the rounded number of deaths attributable to HW_{low}, HW_{middle}, and HW_{high} in Thailand. Deaths from neoplasms and certain infectious and parasitic diseases were the major mortality burdens attributable to HW_{low}, HW_{middle}, and HW_{high}, followed by deaths from diseases of the respiratory system, and deaths from diseases of the circulatory system.

Table 1. Heatwave definitions used in this study

Heatwave types	Specific definitions	Categories
Heatwave type 1	90^{th} percentile & 2 days	Low-intensity heatwaves (HW_{low})
Heatwave type 2	90^{th} percentile & 3 days	
Heatwave type 3	90^{th} percentile & 4 days	
Heatwave type 4	91^{th} percentile & 2 days	
Heatwave type 5	91^{th} percentile & 3 days	
Heatwave type 6	91^{th} percentile & 4 days	
Heatwave type 7	92^{th} percentile & 2 days	
Heatwave type 8	92^{th} percentile & 3 days	
Heatwave type 9	92^{th} percentile & 4 days	
Heatwave type 10	93^{th} percentile & 2 days	
Heatwave type 11	93^{th} percentile & 3 days	
Heatwave type 12	93^{th} percentile & 4 days	
Heatwave type 13	94^{th} percentile & 2 days	Middle-intensity heatwaves (HW_{middle})
Heatwave type 14	94^{th} percentile & 3 days	
Heatwave type 15	94^{th} percentile & 4 days	
Heatwave type 16	95^{th} percentile & 2 days	
Heatwave type 17	95^{th} percentile & 3 days	
Heatwave type 18	95^{th} percentile & 4 days	
Heatwave type 19	96^{th} percentile & 2 days	
Heatwave type 20	96^{th} percentile & 3 days	
Heatwave type 21	96^{th} percentile & 4 days	
Heatwave type 22	97^{th} percentile & 2 days	High-intensity heatwaves (HW_{high})
Heatwave type 23	97^{th} percentile & 3 days	
Heatwave type 24	97^{th} percentile & 4 days	
Heatwave type 25	98^{th} percentile & 2 days	
Heatwave type 26	98^{th} percentile & 3 days	
Heatwave type 27	98^{th} percentile & 4 days	
Heatwave type 28	99^{th} percentile & 2 days	
Heatwave type 29	99^{th} percentile & 3 days	
Heatwave type 30	99^{th} percentile & 4 days	

Table 2. Mean values of daily climatic factors and cause-specific mortality in 60 communities of Thailand, from 1999 to 2008

	T_{max} (°C)	T_{mean} (°C)	T_{min} (°C)	RH (%)	Total	AB	C00D48	C0097	E	E1014	I	I2025	J	J1218	K	N	N1719
Bangkok	33.37	29.26	25.34	70.57	58.31	12.49	15.00	14.90	1.75	1.56	11.63	0.76	7.39	4.34	3.07	2.66	2.27
Nakhon Ratchasima	32.21	27.09	22.28	71.75	19.20	4.02	4.71	4.68	0.82	0.72	3.86	0.32	2.60	1.29	1.26	0.93	0.78
Ubon Ratchathani	33.08	27.53	22.34	71.17	13.43	2.54	3.37	3.35	0.73	0.67	2.22	0.17	1.54	0.75	0.77	1.07	0.96
Khon Kaen	32.75	27.23	22.11	72.03	16.13	2.81	4.38	4.36	1.13	1.07	2.52	0.22	1.67	0.69	1.03	1.15	1.02
Chiang Mai	32.18	26.27	20.68	72.00	19.30	3.93	4.85	4.83	0.73	0.65	3.21	0.30	2.43	1.03	1.14	1.36	1.17
Buriram	32.94	27.43	22.31	8.81	1.80	2.38	2.38	2.37	0.42	0.38	1.39	0.12	1.00	0.48	0.57	0.59	0.51
Udon Thani	32.63	27.13	21.95	72.19	12.02	1.97	3.68	3.67	0.79	0.74	1.85	0.16	1.19	0.48	0.75	0.91	0.82
Nakhon Si Thammarat	32.41	27.62	23.16	78.92	10.66	2.04	2.47	2.46	0.41	0.36	2.34	0.14	1.37	0.56	0.55	0.60	0.50
Surin	32.91	27.54	22.53	72.89	8.78	1.70	2.43	2.43	0.43	0.37	1.47	0.12	0.93	0.47	0.60	0.56	0.50
Songkhla	32.46	27.95	23.85	79.43	9.53	1.94	2.21	2.20	0.38	0.33	1.99	0.15	1.15	0.50	0.54	0.46	0.39
Roi Et	32.25	27.16	22.36	72.29	10.60	1.63	3.34	3.32	0.74	0.71	1.68	0.15	1.04	0.46	0.66	0.76	0.69
Chonburi	32.14	28.41	24.76	74.79	12.89	2.93	2.93	2.92	0.48	0.43	2.58	0.15	1.59	0.78	0.75	0.70	0.60
Chiang Rai	30.94	25.07	19.67	76.78	13.01	2.51	3.19	3.19	0.46	0.40	2.28	0.23	1.60	0.68	0.90	1.05	0.87
Samut Prakan	30.46	28.33	26.26	71.31	8.42	2.00	1.92	1.92	0.29	0.26	1.64	0.18	1.00	0.56	0.49	0.45	0.39
Chaiyaphum	32.96	27.75	22.89	70.03	7.90	1.37	2.43	2.42	0.49	0.45	1.15	0.11	0.82	0.35	0.53	0.55	0.49
Sakon Nakhon	31.81	26.52	21.65	72.97	8.50	1.45	2.72	2.71	0.47	0.44	1.28	0.10	0.77	0.32	0.50	0.72	0.66
Nakhon Sawan	33.78	28.51	23.60	71.41	10.41	2.05	2.27	2.26	0.37	0.33	2.28	0.13	1.36	0.65	0.64	0.57	0.50
Phetchabun	33.57	27.85	22.49	73.76	7.30	1.39	1.70	1.69	0.34	0.31	1.32	0.10	0.94	0.40	0.58	0.48	0.41
Surat Thani	32.04	27.55	23.38	80.86	6.27	1.21	1.48	1.47	0.27	0.24	1.18	0.13	0.86	0.36	0.36	0.34	0.28
Kalasin	32.13	27.34	22.19	70.86	8.27	1.36	2.35	2.34	0.59	0.56	1.24	0.11	0.88	0.38	0.54	0.70	0.63

Maha Sarakham	33.78	27.70	21.97	74.87	6.90	1.26	2.03	2.03	0.49	0.45	0.95	0.10	0.74	0.31	0.43	0.53	0.49
Pathum Thani	33.79	28.84	24.14	70.39	6.34	1.47	1.43	1.42	0.22	0.19	1.32	0.08	0.81	0.46	0.37	0.31	0.26
Nong Khai	32.32	26.96	22.02	74.76	5.62	1.03	1.59	1.58	0.35	0.32	0.84	0.08	0.62	0.28	0.35	0.51	0.47
Nakhon Pathom	33.00	27.91	23.14	74.47	7.16	1.52	1.59	1.59	0.28	0.25	1.52	0.10	0.92	0.50	0.42	0.37	0.31
Suphan Buri	33.57	28.38	23.46	71.99	6.92	1.30	1.49	1.48	0.30	0.27	1.63	0.12	0.86	0.42	0.41	0.36	0.31
Phitsanulok	33.19	27.93	22.92	72.71	8.98	1.92	1.65	1.64	0.30	0.26	2.15	0.14	1.08	0.55	0.53	0.42	0.36
Ratchaburi	33.27	28.08	23.45	72.93	8.60	1.77	1.85	1.84	0.30	0.27	1.77	0.13	1.13	0.58	0.48	0.40	0.34
Phra Nakhon Si Ayutthaya	33.64	28.33	23.29	71.18	6.95	1.49	1.31	1.31	0.23	0.20	1.51	0.10	0.98	0.51	0.42	0.33	0.29
Lampang	33.14	26.80	20.94	72.57	10.13	2.02	2.33	2.32	0.37	0.31	1.94	0.19	1.27	0.55	0.55	0.71	0.63
Lopburi	33.71	28.39	23.42	72.84	8.10	1.76	1.71	1.70	0.25	0.22	1.66	0.09	1.02	0.56	0.51	0.41	0.36
Kamphaeng Phet	33.23	27.96	23.16	77.62	4.02	0.89	0.79	0.79	0.14	0.12	0.78	0.05	0.56	0.26	0.29	0.23	0.20
Narathiwat	31.40	27.33	23.50	81.06	4.42	0.77	0.74	0.73	0.23	0.21	1.05	0.25	0.65	0.26	0.22	0.23	0.19
Nakhon Phanom	31.74	26.40	21.44	75.10	4.57	0.69	1.43	1.42	0.23	0.21	0.65	0.04	0.46	0.19	0.27	0.44	0.40
Chachoengsao	33.11	27.72	22.94	72.58	5.81	1.14	1.28	1.27	0.24	0.22	1.14	0.06	0.82	0.43	0.35	0.32	0.27
Pattani	32.46	27.80	23.57	81.36	3.60	0.64	0.66	0.65	0.20	0.19	0.81	0.18	0.52	0.17	0.15	0.18	0.14
Loei	32.05	26.17	20.76	72.68	3.98	0.67	0.96	0.96	0.22	0.20	0.67	0.06	0.46	0.20	0.27	0.35	0.31
Trang	32.98	27.81	22.95	81.81	3.83	0.72	0.80	0.80	0.13	0.12	0.82	0.05	0.52	0.23	0.19	0.23	0.19
Sukhothai	33.18	27.63	22.43	77.56	5.19	0.94	1.16	1.15	0.21	0.19	0.98	0.08	0.70	0.36	0.32	0.32	0.29
Rayong	32.86	28.69	24.87	74.61	5.24	1.12	1.05	1.05	0.19	0.18	0.99	0.07	0.71	0.37	0.29	0.27	0.24
Phichit	32.75	27.91	23.37	75.26	4.33	0.84	0.90	0.90	0.14	0.12	0.82	0.05	0.59	0.35	0.30	0.26	0.22
Sa Kaeo	33.49	28.34	23.63	75.58	3.88	0.77	0.99	0.98	0.14	0.11	0.64	0.04	0.50	0.26	0.25	0.19	0.16
Tak	31.53	25.82	20.57	75.20	3.33	0.66	0.79	0.79	0.10	0.09	0.59	0.05	0.52	0.23	0.19	0.15	0.13
Chanthaburi	32.90	27.84	23.16	75.75	6.08	1.41	1.39	1.38	0.18	0.15	1.10	0.07	0.80	0.41	0.35	0.30	0.25

Prachuap Khiri Khan	32.34	27.67	23.36	75.89	4.07	0.95	0.95	0.94	0.15	0.13	0.71	0.05	0.55	0.27	0.23	0.23	0.20
Phatthalung	32.26	28.02	24.11	80.00	3.11	0.67	0.73	0.72	0.13	0.12	0.60	0.05	0.42	0.19	0.17	0.17	0.14
Phayao	31.79	25.79	20.33	77.10	6.32	1.41	1.56	1.56	0.23	0.21	1.04	0.09	0.75	0.30	0.39	0.46	0.39
Chumphon	31.89	27.37	23.16	78.69	3.50	0.69	0.77	0.77	0.11	0.09	0.77	0.05	0.53	0.25	0.18	0.16	0.13
Yala	32.99	27.89	23.35	77.42	3.16	0.58	0.58	0.57	0.15	0.14	0.73	0.10	0.40	0.16	0.16	0.15	0.12
Nan	32.01	25.85	20.08	76.37	5.47	0.95	1.23	1.22	0.17	0.15	0.99	0.09	0.89	0.31	0.31	0.45	0.40
Uttaradit	33.83	28.14	22.93	73.68	5.58	1.10	1.20	1.19	0.21	0.18	1.16	0.10	0.75	0.34	0.38	0.31	0.26
Phrae	32.89	27.16	21.97	75.57	6.28	1.15	1.75	1.75	0.29	0.26	1.07	0.12	0.73	0.28	0.38	0.47	0.41
Prachinburi	33.99	28.64	23.76	75.05	4.29	0.92	0.98	0.98	0.13	0.11	0.83	0.05	0.61	0.34	0.28	0.25	0.21
Lamphun	32.90	26.65	20.82	72.91	4.61	0.89	1.17	1.17	0.19	0.17	0.83	0.08	0.56	0.23	0.26	0.37	0.32
Mukdahan	32.90	27.30	22.23	73.57	2.67	0.45	0.62	0.62	0.13	0.12	0.34	0.03	0.25	0.12	0.14	0.20	0.17
Chai Nat	33.21	28.14	23.56	70.28	3.17	0.72	0.69	0.68	0.12	0.11	0.63	0.04	0.42	0.22	0.22	0.15	0.13
Phuket	32.15	28.46	24.94	78.25	2.57	0.60	0.55	0.54	0.10	0.09	0.52	0.03	0.32	0.16	0.16	0.15	0.14
	T_{max}	T_{mean}	T_{min}	RH	Total	AB	C00D48	C0097	E	E1014	I	I2025	J	J1218	K	N	N1719
Satun	32.60	27.96	23.69	79.19	1.20	0.26	0.25	0.25	0.06	0.05	0.26	0.04	0.15	0.06	0.06	0.06	0.05
Mae Hong Son	32.95	26.35	20.35	76.38	1.20	0.27	0.27	0.27	0.04	0.04	0.21	0.03	0.17	0.07	0.07	0.06	0.05
Trat	31.77	27.53	23.57	80.42	2.12	0.43	0.52	0.52	0.08	0.07	0.37	0.03	0.29	0.15	0.13	0.13	0.12
Ranong	32.06	27.76	23.78	79.08	1.11	0.26	0.26	0.26	0.05	0.05	0.23	0.04	0.14	0.07	0.06	0.05	0.05

Tmax, maximum temperature; **Tmean**, mean temperature; **Tmin**, minimum temperature; **RH**, relative humidity; **Total**, total deaths; **AB**, certain infectious and parasitic diseases; **C00D48**, neoplasms; **C0097**, malignant neoplasms; **E**, endocrine, nutritional and metabolic diseases; **E1014**, diabetes mellitus; **I**, diseases of the circulatory system; **I2025**, ischemic heart diseases; **J**, diseases of the respiratory system; **J1218**, pneumonia; **K**, diseases of the digestive system; **N**, diseases of the genitourinary system; **N1719**, renal failure.

Table 3. The pooled acute effects of heatwaves on cause-specific mortality in 60 communities of Thailand, from 1999 to 2008

Disease	Rank	RR (95% CI)$	Rank	RR (95% CI)$	Rank	RR (95% CI)$
		HW_{low}*		HW_{middle}*		HW_{high}*
Total deaths		1.113 (1.097, 1.130)		1.120 (1.103, 1.138)		1.126 (1.103, 1.150)
Certain infectious and parasitic diseases	1	1.183 (1.146, 1.221)	2	1.190 (1.144, 1.238)	2	1.176 (1.114, 1.241)
Ischaemic heart diseases	2	1.171 (1.116,1.229)	1	1.195 (1.137, 1.256)	1	1.219 (1.134, 1.311)
Pneumonia	3	1.150 (1.096, 1.207)	3	1.184 (1.104, 1.269)	3	1.132 (1.032, 1.242)
Malignant neoplasms	4	1.139 (1.101, 1.179)	4	1.138 (1.097, 1.182)	4	1.128 (1.083, 1.175)
Neoplasms	5	1.139 (1.100,1.179)	5	1.137 (1.095, 1.180)	5	1.127 (1.082, 1.174)
Diseases of the digestive system	6	1.132 (1.080, 1.186)	7	1.120 (1.068, 1.173)	7	1.103 (1.038, 1.173)
Endocrine, nutritional and metabolic diseases	7	1.127 (1.077, 1.180)	9	1.103 (1.032, 1.178)	10	1.059 (0.970, 1.156)
Diabetes mellitus	8	1.125 (1.070, 1.182)	6	1.121 (1.053, 1.192)	9	1.074 (0.984, 1.171)
Diseases of the respiratory system	9	1.105 (1.068, 1.143)	8	1.118 (1.070, 1.168)	6	1.116 (1.053, 1.182)
Diseases of the circulatory system	10	1.079 (1.051, 1.108)	10	1.092 (1.063, 1.121)	8	1.095 (1.051, 1.141)
Renal failure	11	1.037 (0.975, 1.103)	12	0.996 (0.928, 1.170)	11	1.038 (0.970, 1.111)
Diseases of the genitourinary system	12	1.036 (0.981, 1.095)	11	1.000 (0.941, 1.062)	12	1.028 (0.967, 1.091)

$ RR, relative risk; CI, confidence interval

* HW_{low}, low-intensity heatwaves; HW_{middle}, middle-intensity heatwaves; HW_{high}, high-intensity heatwaves

Table 4. The pooled cumulative effects of heatwaves on cause-specific mortality in 60 communities of Thailand, from 1999 to 2008

Disease	Rank	RR (95% CI)[$]	Rank	RR (95% CI)[$]	Rank	RR (95% CI)[$]
		HW_{low}[*]		HW_{middle}[*]		HW_{high}[*]
Total deaths		1.169 (1.131, 1.208)		1.155 (1.110, 1.201)		1.126 (1.069, 1.186)
Certain infectious and parasitic diseases	1	1.268 (1.175, 1.369)	1	1.248 (1.145, 1.359)	1	1.203 (1.080, 1.340)
Diabetes mellitus	2	1.260 (1.141, 1.390)	2	1.235 (1.100, 1.386)	7	1.100 (0.943, 1.283)
Neoplasms	3	1.222 (1.132, 1.320)	3	1.200 (1.105, 1.303)	4	1.117 (1.025, 1.218)
Endocrine, nutritional and metabolic diseases	4	1.220 (1.108, 1.344)	5	1.179 (1.057, 1.316)	8	1.093 (0.949, 1.259)
Malignant neoplasms	5	1.211 (1.118, 1.312)	4	1.199 (1.105, 1.302)	2	1.121 (1.030, 1.220)
Ischemic heart diseases	6	1.187 (1.082, 1.301)	6	1.161 (1.045, 1.290)	5	1.106 (0.946, 1.294)
Diseases of the digestive system	7	1.175 (1.087, 1.270)	7	1.136 (1.044, 1.235)	10	1.031 (0.918, 1.157)
Pneumonia	8	1.155 (1.052, 1.267)	9	1.124 (0.997, 1.268)	9	1.084 (0.950, 1.237)
Diseases of the respiratory system	9	1.145 (1.081, 1.212)	10	1.122 (1.043, 1.208)	6	1.102 (1.014, 1.197)
Diseases of the circulatory system	10	1.129 (1.070, 1.190)	8	1.129 (1.062, 1.200)	3	1.119 (1.019, 1.228)
Diseases of the genitourinary system	11	1.012 (0.937, 1.092)	11	0.946 (0.853, 1.049)	11	0.904 (0.795, 1.027)
Renal failure	12	1.010 (0.910, 1.121)	12	0.901 (0.788, 1.031)	12	(0.752, 1.004)

[$] RR, relative risk; CI, confidence interval

[*] HW_{low}, low-intensity heatwaves; HW_{middle}, middle-intensity heatwaves; HW_{high}, high-intensity heatwaves

Table 5. The number of deaths attributable to heatwaves in Thailand under optimal lags (cumulative), from 1999 to 2008

Disease	Rank	Attributable number	Rank	Attributable number	Rank	Attributable number
		HW_{low}*		HW_{middle}*		HW_{high}*
Total deaths		19686		12329		5687
Neoplasms	1	6622	1	3977	1	1867
Malignant neoplasms	2	6544	2	3926	2	1813
Certain infectious and parasitic diseases	3	4566	3	3199	3	1345
Diseases of the respiratory system	4	2751	5	1569	5	781
Diseases of the circulatory system	5	2556	4	2125	4	1081
Pneumonia	6	1480	6	1000	7	433
Endocrine, nutritional and metabolic diseases	7	1364	7	859	8	430
Ischemic heart diseases	8	1341	8	837	6	576
Diabetes mellitus	9	1147	9	694	9	377
Diseases of the digestive system	10	1091	10	608	10	313
Diseases of the genitourinary system	11	512	11	231	11	127
Renal failure	12	464	12	175	12	110

*HW_{low}, low-intensity heatwaves; HW_{middle}, middle-intensity heatwaves; HW_{high}, high-intensity heatwaves. The national attributable number was calculated by summing up all regional specific estimates (refer to equations described in the Methods section).

Spatial distribution of the heatwave effects on mortality

Figure 1 illustrated the acute effects of HW_{low}, HW_{middle}, and HW_{high} on total deaths across different provinces. We found that the effects of HW_{low} on total deaths in provinces in Northern and Central Thailand (e.g., Kamphaeng Phet, and Nakhon Sawan) were the highest, and the geographical scale spread when heatwave intensity increased from HW_{low} to HW_{middle} (Phichit, Chai Nat, and Suphan Buri) and HW_{high}. Interestingly, we also observed that there were provinces which were vulnerable to HW_{low} and/or HW_{middle}, but not to HW_{high} (e.g., Prachuap Khiri Khan, and Yala). Figure S3 (supplementary material) illustrated the effects of HW_{low}, HW_{middle}, and HW_{high} on cause-specific deaths across different provinces of Thailand, implying that heatwave-vulnerable provinces varied by cause and heatwave intensity.

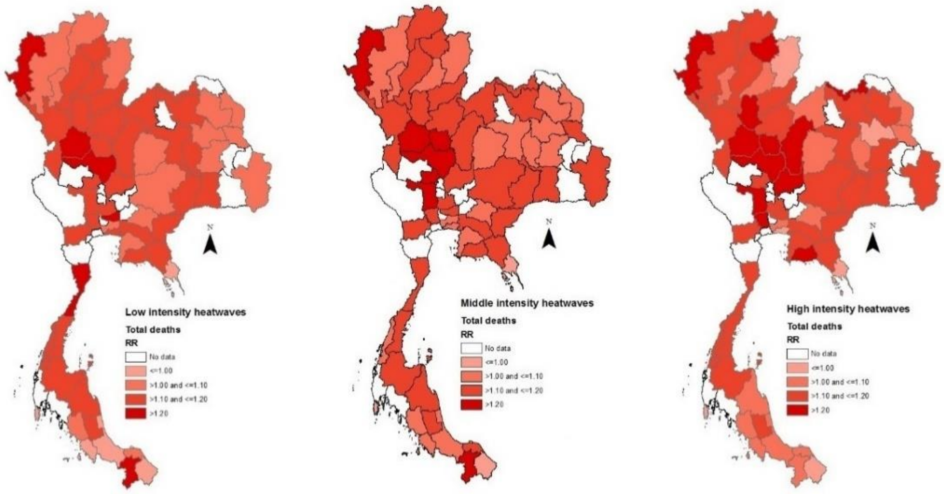


Figure 1. Heatwave effects on total deaths in 60 Thailand provinces

Factors contributing to the heterogeneity of heatwave effects across different provinces

Figure 2 showed the factors contributing to the heterogeneity of the acute effects of heatwaves on total deaths across different provinces. Table S2 (supplementary material) presented the details of the Cochran Q test and I^2 statistic. For HW_{low}, a higher latitude, a lower longitude, and a higher proportion of the elderly, corresponded to a greater effect of heatwaves on total deaths. For HW_{middle}, a lower relative humidity, lower educational attainment, and a higher proportion of elderly people corresponding to a greater effect of heatwaves on total deaths. For HW_{high}, no factors significantly contributed to the heterogeneity, suggesting that all subgroups were vulnerable to HW_{high}. Figure S4 (supplementary material) showed the factors contributing to the heterogeneity of the effects of heatwaves on cause-specific deaths across different provinces, suggesting that the proportion of the elderly was the most consistent factor influencing people's vulnerability to heatwaves across different provinces.

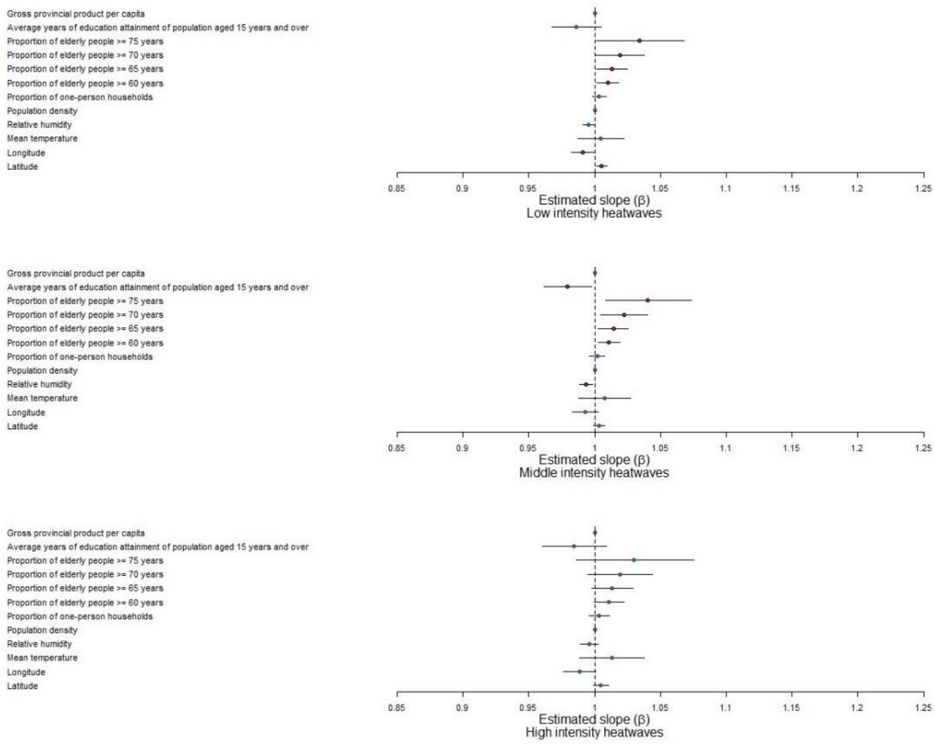


Figure 2. Factors contributing to the spatial heterogeneity of heatwave effects

Discussion

This study, for the first time, grouped the most widely used heatwave definitions into three categories and quantified the mortality burden attributable to heatwaves in Thailand after incorporating evidence-based lags. It has yielded several notable findings: 1). The acute effect of heatwaves on total deaths increased when heatwave intensity increased, but this pattern did not apply to cause-specific deaths, and interestingly, the cumulative effects of heatwaves on total and cause-specific deaths decreased when heatwave intensity increased (Table 4); 2). The acute and cumulative effects of HW_{low}, HW_{middle} and HW_{high} on deaths from certain infectious and parasitic diseases and neoplasms ranked among the highest, causing considerable mortality burden; 3). HW_{low} and HW_{middle} effects on deaths from endocrine, nutritional and metabolic diseases (e.g., diabetes mellitus) may last way beyond one to two days.

On the contrary, the effects of HW_{low}, HW_{middle} and HW_{high} on the commonly recognized heatwave-related death causes, such as ischaemic heart diseases and pneumonia, seemed to occur more rapidly; 4). Deaths from diseases of the circulatory system and diseases of the respiratory system appeared to be more sensitive to HW_{high} (Table 4), but HW_{low} and HW_{middle} also caused substantial mortality burden from diseases of the circulatory system and diseases of the respiratory system, due to the high prevalence of these diseases; 5). The effects of HW_{low}, HW_{middle}, and HW_{high} on total deaths were the highest in provinces of Western Thailand. Further, this heatwave-vulnerable region spread to Midwestern Thailand when heatwave intensity increased from HW_{low} and HW_{middle} to HW_{high}; 6). The proportion of the elderly population was the most consistent factor which contributed to the spatial heterogeneity of heatwave effects, and education attainment, relative humidity, and latitude may also play a role in influencing the heatwave vulnerability across different provinces.

There is evidence suggesting that mild heat caused more mortality burden (attributable fraction) than extreme heat globally because mild heat occurred much more frequently than extreme heat [7]. In our study, surprisingly, we found that in Thailand mild heatwaves (HW_{low} and HW_{middle}) not just caused more mortality burden (i.e., attributable fraction and attributable death number) than extreme heatwaves (HW_{high}) (Table 5), but also had greater cumulative effects (i.e., RR) on total and cause-specific mortality (Table 4), although the acute effect of heatwaves on total mortality increased with heatwave intensity (Table 3). A study of Guo et al. which examined how heatwaves affected mortality acutely in 18 countries/regions (including Thailand) using 90th, 92.5th, 95th and 97.5th as the temperature thresholds to define heatwaves observed that the effect of heat waves on total mortality was higher when using higher temperature thresholds [10]. Our finding on the acute effect of heatwaves on total mortality echoed the finding of Guo et al., and proved their argument that this finding might be driven by the fact that the acute effect of heatwaves on deaths from diseases of the circulatory system increased with heatwave intensity (Table 3) [32]. Nevertheless, our findings also call for attention to the greater cumulative effects of mild heatwaves on total and cause-specific mortality than extreme heatwaves given that these mild heatwaves happened much more frequently, and this finding might partially be explained by the longer harvesting effect of extreme heatwaves [10].

Although the past few decades have witnessed declining rates of infectious, maternal, neonatal, and nutritional diseases globally, neoplasms and infectious diseases still caused a huge disease burden, especially in under-developed countries [33, 34]. In this study, we observed the considerable acute and cumulative effects of heatwaves on deaths from neoplasms and certain infectious and parasitic diseases under all different intensity heatwaves, indicating that future burden of neoplasms and infectious and parasitic diseases due to heatwaves may keep increasing as heatwaves will become more frequent, more intense and longer-lasting [3]. It is delightful that Global Burden of Disease Risk Factor Collaborators will add temperature as a risk factor in their future work given the massive health effects of climate change and the increasing global policy focus on this field [35]. Previous studies have found increases in deaths from neoplasms during heatwaves in Belgrade (Serbia) [36], Essen (Germany) [37], Catalonia (Spain) [5], and the Netherlands [38], and they attributed this increase to short-term harvesting effect. Our findings on the acute and cumulative effects of heatwaves on deaths from neoplasm suggested that heatwaves may trigger existing issues of cancer patients, and the reasons behind the effect of heat waves on neoplasm warrant more research attention. The underlying mechanisms of heatwave effects on infectious diseases (e.g., intestinal infectious diseases) have been well documented in the existing literature. High temperature promotes the growth of bacteria [39], affects food chain [40], and alters people's hygiene behaviour [41]. The increase in infectious diseases during heatwaves also remind the health sector of infectious disease control and prevention in Thailand to be better prepared in the face of heatwaves.

In this study, we found that acute effect of heatwaves on deaths from endocrine, nutritional and metabolic diseases was not high, but the cumulative effects of HW_{low} and HW_{middle} on deaths from endocrine, nutritional and metabolic diseases (especially diabetes mellitus) ranked very high amongst all death causes. This implies that the control and prevention of heatwave-related deaths from endocrine, nutritional and metabolic diseases rely not just on heatwave early warning but also upon a constant protection on patients with pre-existing severe endocrine, nutritional and metabolic diseases before, during and after heatwaves. The compromised thermoregulatory function of diabetic patients due to autonomic neuropathy [42], as well as the effects of high temperature on glucose tolerance [43] and insulin absorption [44], may explain the effect of heat waves on deaths from diabetes. We noticed that, different from endocrine, nutritional and metabolic diseases, effects of HW_{low}, HW_{middle}, and HW_{high} on deaths from ischaemic heart diseases and pneumonia occurred relatively acutely. The physiological mechanisms explaining the effects of heatwaves on ischaemic heart diseases and pneumonia have been widely described [45-47]. Briefly, increased respiratory and heart rate, and increased surface blood circulation etc., put extra pressure on cardiovascular and respiratory systems, triggering the deaths of those patients with pre-existing severe ischaemic heart diseases or pneumonia. Ischaemic heart diseases have been the number one cause of years of life lost in Thailand in 2016 [33], and our finding reminds the caretakers of patients with severe ischaemic heart diseases or pneumonia to take protective measures (e.g., let those patients stay in cool places and stay hydrated) on heatwaves days.

For the acute effect of heatwaves on total mortality, the vulnerable provinces were largely located in Western Thailand, and the geographical scale of heatwave-vulnerable region spread to Midwestern Thailand when heatwave intensity increased to HW_{high}, indicating that heatwave prevention sources may need to be more allocated to Western or Midwestern Thailand. Nevertheless, the acute effect of heatwaves on total mortality in some provinces (e.g., Prachuap Khiri Khan, and Yala) decreased when heatwave intensity increased to HW_{high}, and the geographical distribution of heatwave vulnerability varied by cause of death, highlighting that province-specific heatwave early warning might be optimal for Thailand. In terms of the drivers behind the spatial heterogeneity in heatwave vulnerability, we found that higher proportion of the elderly population was associated with greater heatwave vulnerability. The greater heat/heatwave sensitivity in the elderly population has been extensively reported [6, 48], which may be largely due to their compromised thermoregulatory function because of their insufficient increase in cardiac output and less redistribution of blood flow from renal and splanchnic circulations etc. [49]. Our finding suggests that heatwave prevention strategies in Thailand focusing on elderly people protection may largely relieve heatwave-related mortality burden and improve public health. In this study, we have also noticed that better education attainment was associated with a lower heatwave vulnerability, which is consistent with a study conducted in Guangdong, China [50], but inconsistent with another study conducted in 66 communities in China [6]. We speculate that better education attainment may raise the awareness of heatwave threat or conception of proper prevention measures. Also, education attainment might be a proxy of socioeconomic status as people living in poverty may not have enough access to good education in under-developed countries, although in this study we cannot testify this hypothesis because of the lack of GPPPC data in the year 2000. It has also been observed that low relative humidity contributed to greater heatwave vulnerability in this study. The popular scientific opinion is that high relative humidity during heatwaves may make people suffer more as people cannot sweat properly when relative humidity is too high, although the exact role relative humidity plays in the relationship between ambient temperature/heatwave and human health remains largely unclear so far [51].

This study has several strengths. First, for the first time, 30 heatwave definitions covering all widely used heatwave intensities and durations were grouped into three heatwave categories, allowing us to comprehensively understand how low-intensity heatwaves, middle intensity heatwaves and high-intensity heatwaves affected mortality. Second, GCV was used to identify the optimal lags for each province/cause-specific mortality, which made it possible not just to assess the acute effect of heatwaves on mortality, but also accurately and adequately quantify the mortality burden attributable to different heatwaves. Third, this is, to the best of our knowledge, the most comprehensive study examining how heatwaves affected total and cause-specific mortality using the data from most provinces of Thailand.

Several limitations of this study also need to be acknowledged. First, due to data availability issue, no air pollutants were controlled for in the model, although research in the US found temperature effects on mortality may be robust to air pollutants [52]. Second, the data that we used were from the year 1999 to the year 2008, and heatwave sensitivity in Thailand population may change from 2009 until now, although this is the best data set so far. Third, data on GPPPC during the study period were not available, and we used GPPPC in the year 2013 as a proxy, restricting us to examine better whether economic factor modified the effect of heat waves on mortality in Thailand.

Conclusions

Mild heatwaves were associated with greater cumulative effects on total and cause-specific mortality in Thailand than extreme heatwaves. Heatwave-related mortality burden from neoplasms and infectious diseases may continue to increase in the future as climate change proceeds, and province-specific and tailored heatwave prevention strategies are focusing on the elderly population may relieve heatwave-related health burden in Thailand. This study calls for more in-depth investigations which quantify health effects of different intensity heatwaves incorporating an evidence-based lag structure in other countries/regions.

References

1. Watts, N.; Amann, M.; Ayeb-Karlsson, S.; Belesova, K.; Bouley, T.; Boykoff, M.; Byass, P.; Cai, W.; Campbell-Lendrum, D.; et al., The Lancet Countdown on health and climate change: from 25 years of inaction to a global transformation for public health. *Lancet* **2018**, 391, (10120), 581-630.
2. Wang, H.; Horton, R., Tackling climate change: the greatest opportunity for global health. *The Lancet* 386, (10006), 1798-1799.
3. IPCC, Climate change 2014: synthesis report. Contribution of working groups I, II and III to the fifth assessment report of the intergovernmental panel on climate change. In Geneva, Switzerland 2014.
4. Anderson, B.; Bell, M. L., Heat waves in the United States: mortality risk during heat waves and effect modification by heat wave characteristics in 43 U.S. communities. *Environ Health Perspect* **2011**, 119, (2), 210-218.
5. Basagaña, X.; Sartini, C.; Barrera-Gómez, J.; Dadvand, P.; Cunillera, J.; Ostro, B.; Sunyer, J.; Medina-Ramón, M., Heat Waves and Cause-specific Mortality at all Ages. Epidemiology 2011, 22, (6), 765-772.
6. Ma, W.; Zeng, W.; Zhou, M.; Wang, L.; Rutherford, S.; Lin, H.; Liu, T.; Zhang, Y.; Xiao, J.; Zhang, Y.; Wang, X.; Gu, X.; Chu, C., The short-term effect of heat waves on mortality and its modifiers in China: An analysis from 66 communities. Environ Int 2015, 75, (Supplement C), 103-109.
7. Gasparrini, A.; Guo, Y.; Hashizume, M.; Lavigne, E.; Zanobetti, A.; Schwartz, J.; Tobias, A.; Tong, S.; Rocklöv, J.; et al., Mortality risk attributable to high and low ambient temperature: a multicountry observational study. Lancet 2015, 386, (9991), 369-75.
8. Xu, Z.; FitzGerald, G.; Guo, Y.; Jalaludin, B.; Tong, S., Impact of heatwave on mortality under different heatwave definitions: A systematic review and meta-analysis. Environ Int 2016, 89–90, 193-203.
9. Tong, S.; Wang, X. Y.; Barnett, A. G., Assessment of Heat-Related Health Impacts in Brisbane, Australia: Comparison of Different Heatwave Definitions. PLoS ONE 2010, 5, (8), e12155.
10. Guo, Y.; Gasparrini, A.; Armstrong, B.; Tawatsupa, B.; Tobias, A.; Lavigne, E.; Coelho, M.; Pan, X.; Kim, H.; et al., Heat wave and mortality: A multicountry, multicommunity study. Environ Health Persp 2017, 125, (8), 087006.
11. Tong, S.; Wang, X. Y.; FitzGerald, G.; McRae, D.; Neville, G.; Tippett, V.; Aitken, P.; Verrall, K., Development of health risk-based metrics for defining a heatwave: a time series study in Brisbane, Australia. BMC Public Health 2014, 14, (1), 435.
12. Hajat, S.; Armstrong, B. G.; Nelson, G.; Wilkinson, P., Mortality Displacement of Heat-Related Deaths: A Comparison of Delhi, São Paulo, and London. Epidemiology 2005, 16, (5), 613-620.
13. Baccini, M.; Kosatsky, T.; Biggeri, A., Impact of Summer Heat on Urban Population Mortality in Europe during the 1990s: An Evaluation of Years of Life Lost Adjusted for Harvesting. PLOS ONE 2013, 8, (7), e69638.
14. Schifano, P.; Cappai, G.; De Sario, M.; Michelozzi, P.; Marino, C.; Bargagli, A. M.; Perucci, C. A., Susceptibility to heat wave-related mortality: a follow-up study of a cohort of elderly in Rome. Environ Health-Glob 2009, 8, (1), 50.
15. Huang, C.; Barnett, A.; Xu, Z.; Chu, C.; Wang, X.; Turner, L.; Tong, S., Managing the health effects of temperature in response to climate change: challenges ahead. Environ Health Perspect 2013, 121, (4), 415-419.
16. Hertel, S.; Le Tertre, A.; Jöckel, K.-H.; Hoffmann, B., Quantification of the heat wave effect on cause-specific mortality in Essen, Germany. Eur J Epidemiol 2009, 24, (8), 407-414.

17. Benmarhnia, T.; Deguen, S.; Kaufman, J. S.; Smargiassi, A., Review Article: Vulnerability to Heat-related Mortality: A Systematic Review, Meta-analysis, and Meta-regression Analysis. Epidemiology 2015, 26, (6), 781-793.
18. Robinson, P. J., On the Definition of a Heat Wave. Journal of Applied Meteorology 2001, 40, (4), 762-775.
19. Guo, Y.; Punnasiri, K.; Tong, S., Effects of temperature on mortality in Chiang Mai city, Thailand: a time series study. Environ Health-Glob 2012, 11, (1), 36.
20. National Statistical Office, M. o. I. a. C. T., Thailand. http://web.nso.go.th/en/census/poph/cen_poph.htm. (27th November),
21. (NESDB), O. o. t. N. E. a. S. D. B., Gross Regional and Provincial Product, 2013 Edition. In 2015.
22. Nairn, J.; Fawcett, R., The Excess Heat Factor: A Metric for Heatwave Intensity and Its Use in Classifying Heatwave Severity. Int J Env Res Pub He 2015, 12, (1), 227.
23. Wang, Y.; Nordio, F.; Nairn, J.; Zanobetti, A.; Schwartz, J. D., Accounting for adaptation and intensity in projecting heat wave-related mortality. Environ Res 2018, 161, 464-471.
24. Cheng, J.; Xu, Z.; Bambrick, H.; Su, H.; Tong, S.; Hu, W., The mortality burden of hourly temperature variability in five capital cities, Australia: Time-series and meta-regression analysis. Environ Int 2017, 109, (Supplement C), 10-19.
25. Gasparrini, A.; Armstrong, B.; Kovats, S.; Wilkinson, P., The effect of high temperatures on cause-specific mortality in England and Wales. Occup Environ Med 2012, 69, (1), 56-61.
26. Bhaskaran, K.; Gasparrini, A.; Hajat, S.; Smeeth, L.; Armstrong, B., Time series regression studies in environmental epidemiology. Int J Epidemiol 2013, 42, (4), 1187-1195.
27. Xu, Z.; Tong, S., Decompose the association between heatwave and mortality: Which type of heatwave is more detrimental? Environ Res 2017, 156, (Supplement C), 770-774.
28. Gasparrini, A.; Armstrong, B.; Kenward, M. G., Distributed lag non-linear models. Stat Med 2010, 29.
29. Cheng, J.; Xu, Z.; Bambrick, H.; Su, H.; Tong, S.; Hu, W., Heatwave and elderly mortality: An evaluation of death burden and health costs considering short-term mortality displacement Environ Int 2018, 115, 334-342.
30. Viechtbauer, W., Conducting Meta-Analyses in R with the metafor Package. Journal of Statistical Software 2010, 36, (3), 1-48.
31. Gasparrini, A., Distributed lag linear and non-linear models in R: The package dlnm. Journal of Statistical Software 2011, 43, (8), 1-20.
32. Madaniyazi, L.; Zhou, Y.; Li, S.; Williams, G.; Jaakkola, J. J. K.; Liang, X.; Liu, Y.; Wu, S.; Guo, Y., Outdoor Temperature, Heart Rate and Blood Pressure in Chinese Adults: Effect Modification by Individual Characteristics. Sci Rep 2016, 6, 21003.
33. Collaborators, G. C. o. D., Global, regional, and national age-sex specific mortality for 264 causes of death, 1980–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet 2017, 390, (10100), 1151-1210.
34. Collaborators, G. D. a. H., Global, regional, and national disability-adjusted life-years (DALYs) for 333 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet 2017, 390, (10100), 1260-1344.
35. Gakidou, E.; Afshin, A.; Abajobir, A. A.; Abate, K. H.; Abbafati, C.; Abbas, K. M.; Abd-Allah, F.; Abdulle, A. M.; Abera, S. F.; et al., Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet 2017, 390, (10100), 1345-1422.

36. Bogdanović, D.; Milosević, Z.; Lazarević, K.; Dolićanin, Z.; Randelović, D.; Bogdanović, S., The impact of the July 2007 heat wave on daily mortality in Belgrade, Serbia. Central European Journal of Public Health 2013, 21, (3), 140-5.
37. Hoffmann, B.; Hertel, S.; Boes, T.; Weiland, D.; Jöckel, K., Increased cause-specific mortality associated with 2003 heat wave in Essen, Germany. Journal of Toxicology and Environmental Health, Part A 2008, 71, (11-12), 759-65.
38. Huynen, M.; Martens, P.; Schram, D.; Weijenberg, M.; Kunst, A., The impact of heat waves and cold spells on mortality rates in the Dutch population. Environ Health Persp 2001, 109, (5), 463-70.
39. 39. Hashimoto, M.; Fukuda, T.; Shimizu, T.; Watanabe, S.; Watanuki, S.; Eto, Y.; Urashima, M., Influence of climate factors on emergency visits for childhood asthma attack. Pediatrics International 2004, 46, (1), 48-52.
40. D'Souza, R. M.; Becker, N. G.; Hall, G.; Moodie, K. B. A., Does Ambient Temperature Affect Foodborne Disease? Epidemiology 2004, 15, (1), 86-92.
41. Xu, Z.; Liu, Y.; Ma, Z.; Toloo, G.; Hu, W.; Tong, S., Assessment of the temperature effect on childhood diarrhea using satellite imagery. Sci Rep 2014, 4, 5389.
42. Sun, P. C.; Lin, H. D.; Jao, S. H.; Chan, R. C.; Kao, M. J.; Cheng, C. K., Thermoregulatory sudomotor dysfunction and diabetic neuropathy develop in parallel in at-risk feet. Diabetic Medicine 2008, 25, (4), 413-418.
43. Akanji, A. O.; Oputa, R. A., The effect of ambient temperature on glucose tolerance and its implications for the Tropics. Tropical and Geographical Medicine 1991, 43, (3), 283-287.
44. Koivisto, V. A.; Fortney, S.; Hendler, R.; Felig, P., A rise in ambient temperature augments insulin absorption in diabetic patients. Metabolism 1981, 30, (4), 402-405.
45. Chen, K.; Bi, J.; Chen, J.; Chen, X.; Huang, L.; Zhou, L., Influence of heat wave definitions to the added effect of heat waves on daily mortality in Nanjing, China. Sci Total Environ 2015, 506-507, (Supplement C), 18-25.
46. Oudin Åström, D.; Schifano, P.; Asta, F.; Lallo, A.; Michelozzi, P.; Rocklöv, J.; Forsberg, B., The effect of heat waves on mortality in susceptible groups: a cohort study of a mediterranean and a northern European City. Environ Health-Glob 2015, 14, (1), 30.
47. Xu, Z.; Liu, Y.; Ma, Z.; Li, S.; Hu, W.; Tong, S., Impact of temperature on childhood pneumonia estimated from satellite remote sensing. Environ Res 2014, 132, (Supplement C), 334-341.
48. Arbuthnott, K. G.; Hajat, S., The health effects of hotter summers and heat waves in the population of the United Kingdom: a review of the evidence. Environ Health-Glob 2017, 16, (1), 119.
49. Basu, R., High ambient temperature and mortality: a review of epidemiologic studies from 2001 to 2008. Environ Health 2009, 8, 40.
50. Liu, T.; Xu, Y. J.; Zhang, Y. H.; Yan, Q. H.; Song, X. L.; Xie, H. Y.; Luo, Y.; Rutherford, S.; Chu, C.; Lin, H. L.; Ma, W. J., Associations between risk perception, spontaneous adaptation behavior to heat waves and heatstroke in Guangdong province, China. BMC Public Health 2013, 13, (1), 913.
51. Zeng, J.; Zhang, X.; Yang, J.; Bao, J.; Xiang, H.; Dear, K.; Liu, Q.; Lin, S.; Lawrence, W.; Lin, A.; Huang, C., Humidity May Modify the Relationship between Temperature and Cardiovascular Mortality in Zhejiang Province, China. Int J Env Res Pub He 2017, 14, (11), 1383.
52. Anderson, B.; Bell, M., Weather-related mortality: how heat, cold, and heat waves affect mortality in the United States. Epidemiology 2009, 20, (2), 205-213.

2.10 Preparing the next generation of health professionals to tackle climate change: Are China's medical students ready?

Wenmin Liao [1,#], Lianping Yang [1,#], Shuang Zhong [2], Jeremy J. Hess [3], Qiong Wang [1], Junzhe Bao [1],Cunrui Huang [a,]

[1] School of Public Health, Sun Yat-sen University, Guangzhou, China
[2] Center for Chinese Public Administration Research, School of Government, Sun Yat-Sen University, Guangzhou, China
[3] Departments of Emergency Medicine, Environmental and Occupational Health Sciences, and Global Health, Schools of Medicine and Public Health, University of Washington, Seattle, WA, USA
[#] These authors contributed equally to this work.
[*] Correspondence: huangcr@mail.sysu.edu.cn (C. H.).

Liao W, Yang L, Zhong S, Hess JJ, Wang Q, Bao J, et al. Preparing the next generation of health professionals to tackle climate change: Are China's medical students ready? Environmental Research 2019;168:270-277.

Abstract:

Background: Climate change is the biggest global health threat of the 21st century. Medical students will lead the health sector responses and adaptation efforts in the near future, yet little is known in China about their knowledge, perceptions and preparedness to meet these challenges.

Methods: A nationwide study was conducted at five medical universities across different regions of China using a two-stage stratified cluster sampling design. A self-administered questionnaire was applied to collect the information including perception, preparedness and educational needs in response to climate change. The data were first analyzed descriptively, then chi-square tests and Kruskal Wallis tests were applied to determined differences among subgroups, and logistic regression analysis was deployed to detect the socio-demographic factors influencing student's perception.

Results: A total of 1,436 medical students were approached and 1,387 participated in the study (96.6% response rate). Most students were aware of the health impacts because of climate change, with over 90% perceived air quality-related and heat-related illness, while only a small part identified undernutrition and mental health. Approximately 90% embraced their role in tackling climate change, but 50% reported themselves and the health sectors were not adequately prepared. Compared to clinical students, preventive medicine students were more likely to perceive their responsibility to address climate change (OR:1.36, 95% CI: 1.04, 1.78). Also, 80% of students admitted insufficient information and knowledge on climate change and health. Most students agreed that climate change and its health impacts should be included in their current curriculum.

Conclusions: Medical students in China were aware of climate change and felt responsible, but they were not ready to make responses to its health impacts. Educational efforts should reinforce eco-medical literacy development and capacity building in the era of climate change.

Keywords: Climate change; Health impact; Medical student; Perception; Education

Introduction

Climate change is now regarded as the biggest global health problem requiring health sector preparedness [1, 2]. Its effects are already being observed in China, and future projections represent an unacceptably high and potentially catastrophic risk to human health [3]. Climate change affects human health through a wide range of hazardous exposures, including extreme weather events, altered air quality, shifting patterns of infectious disease, as well as sea level rise, ocean acidification, conflict and migration [4]. Given the inertia of the climate system, an increase in hazardous exposures associated with climate change is unavoidable [5], though ultimately health impacts will depend substantially on the degree of effective adaptation. Notably, the impacts of climate change will be concentrated in poorer and vulnerable populations, where climate-sensitive diseases are common, exacerbating existing health inequalities, and stressing the health sector further in these regions [6].

Health professionals have a clear duty and obligation to lead the efforts to protect health from climate change [2, 7, 8]. Similar to leadership in response to other emerging threats, health professionals confronting climate change can highlight the interconnectedness of climate change and health, advocate environmentally sustainable approaches to health services, promote health benefits of mitigation policies, provide healthcare for affected populations, facilitate the building of community resilience, monitor emerging hazards and conduct research to appraise evidence to support adaptation [8-12].

While health professionals are vital to the climate actions, previous studies have found that the health community is ill-prepared to detect, prevent or ameliorate climate-related health problems and craft planned adaptations [13]. Most importantly, the health sector in many countries has not yet made climate change preparedness a priority.

To cope with the health impacts of climate change, engaging medical students is a critical initiative. In China, population health activities are managed by health professionals who have received clinical medicine, preventive medicine or nursing training. The current generation of medical students will practice from the 2020s to the 2060s where climate change-related health impacts emerges. Their efficiency in coping with this biggest challenge of the century may depend on the expertise and skills acquired from their present educational training. Therefore, understanding current medical students' perception and capacity in response to climate change are of great significance in educational planning. To date, there is little literature to rely on, and there is no research in China for appropriate educational innovations. This study aims to answer three questions: First, to what extent do Chinese medical students perceive climate change and its health impacts? Second, how do the medical students perceive their roles in coping with climate change? Third, what are the information, education and training needs identified by the medical students?

Materials and Methods

Data collection

We conducted an anonymous written survey among a sample of Chinese medical students from five universities with medical colleges. A sampling frame was designed to capture data from all regions of the country, and a two-stage stratified cluster sampling design was applied in this study. Firstly, we divided mainland China into five parts including north, west, south, east, and central part with the consideration of geographic and climatic variation, and with one top medical university purposively selected in each part. The selected universities are Harbin Medical University in Harbin, Sichuan University in Chengdu, Sun Yat-sen University in Guangzhou, Fujian Medical University in Fuzhou and Huazhong University of Science and Technology in Wuhan. Secondly, in each selected university, we used cluster sampling and randomly selected around 250 medical students (clinical medicine, preventive medicine or nursing students) from third or fourth grade by taking the whole class as a unit.

This study was approved by the medical ethics committee of the School of Public Health, Sun Yat-sen University. Written informed consent was obtained from study participants. From March to May 2017, the study participants were gathered in a classroom by taking a class as a unit, and it took about 10-15 minutes for them to complete the self-administered questionnaire. The integrity of the return questionnaire was checked by our investigators in the field. This study was a one-time survey, and there was no follow-up.

Survey instrument

A draft questionnaire was developed based on existing literature [13-17]. We then conducted a focus group discussion with 6 non-selected students and administered a draft survey to 30 non-selected students to improve its content validity and to calculate the sample size.

The final version of the questionnaire comprised 33 questions in four parts. The first part of the questionnaire asked questions about perceptions of climate change and its health impacts. Four main questions assessed general perceptions and knowledge regarding climate change and health. Next, to compare the difference between unprompted and prompted responses, two open-ended questions and two lists of closed-ended questions about the specific health issues and vulnerable populations were presented. Then, three questions were presented to assess the students' perceptions of the magnitude of climatic health threats. For close-ended questions in this part, a score of one point was given each time a student identified a health impact or identified a vulnerable group. We accumulated the sum scores of each student and performed Kruskal Wallis tests for original scores to detect the difference between sub-groups. After that, we took the mean score as the cut-off point to categorize their perceptions on health impacts and vulnerable groups into high or low groups, respectively. The second part of the questionnaire was composed of six questions on the responsibilities, abilities, and preparedness of medical students or the health sector to address health-related impacts. These questions used a Likert scale, with a range of –3 (strongly disagree) to 3 (strongly agree) as response options, with no neutral midpoint. For questions in this part, a score of one point was given each time a student expresses a positive attitude (including “mildly agree”, “somewhat agree” and “strongly agree”). We did subgroup analysis using Kruskal Wallis tests and then categorized their perceptions on responsibilities and abilities into high or low groups with the same approach above. The third part of the questionnaire asked ten questions on information, education, and training needs for helping the health sector address climate change and its health impacts. And the last part collected demographic information of respondents, including gender, major, the location of hometown, per capita income of the family and self-rated health status. According to National Bureau of Statistics of China, we divided hometown location of surveyed students into east, central, west and northeast region by taking geographic, climatic conditions and socioeconomic development status into consideration [18].

Statistical analyses

Data of valid questionnaire (missing value less than 3) were double-entered using Epidata 3.1 and then imported into STATA statistical software (version 14.0, STATA Corp) for analysis. First, responses were analyzed descriptively. Second, chi-square tests or Kruskal Wallis tests were applied to determine differences among participant subgroups. Third, several unconditional logistic regression models were deployed to detect the potential influence factors of medical students’ perceptions on health impacts, on vulnerable groups and their responsibilities and abilities (0=low perception, 1=high perception). All statistical analyses we applied were two-sided, and we considered p-values <0.05 as statistically significant. Missing data (accounting $<0.5\%$) were not involved in the analysis.

Results

A total of 1,436 students were approached, and 1,387 valid questionnaires were collected in the study (response rate, 96.6%). Approximately a quintile of the participants (n=260) belonged to each surveyed university. Most participants were female, with per capita income of family ranging from US$ 300-749 monthly. The average age of students was 21.8 years old (ranging from 17 to 28). Most students (83.8%) assessed their health status as good or beyond (Table 1).

Perceptions of climate change and its health impacts

In this study, 68% of students agreed that the process of climate change is controllable through effective mitigation and adaptation. Preventive medicine students were more likely to believe climate change is controllable than clinical medicine and nursing students (see Supplemental Material, Table S1).

Table 1. Summary statistics of participant information

Characteristic	N	Percentage (%)
Total	1,387	100.0
Gender		
Male	461	33.2
Female	926	66.8
University		
Sun Yat-sen University	331	22.4
Huazhong University of Science and Technology	248	17.9
Sichuan University	262	18.9
Fujian Medical University	258	18.6
Harbin Medical University	308	22.2
Major		
Clinical medicine	644	46.4
Preventive medicine	430	31.0
Nursing	313	22.6
Location of hometown		
Central China	304	22.1
Eastern China	506	36.8
Western China	219	15.9
Northeastern China	345	25.1
Per capital income of family		
<\$150	154	11.1
\$150-299	284	20.5
\$300-749	514	37.1
\$750-1499	293	21.1
≥\$1500	127	9.2
Self-rated health status		
Very good	303	21.9
Good	858	61.9
Medium	208	15.0
Poor	18	1.3

When asked whether climate change and its health impacts would overall have net beneficial or detrimental effects, the majority of students stated that climate change and its health-related impacts are detrimental, with 17.4% identifying climate change as "very bad" and 13.4% identifying the health impacts of climate change as "very bad" (Figure 1). Females were significantly more likely than males to identify climate change and its health-related impacts as a "bad" thing (χ^2=32.87, p<0.01, and χ2=26.02, p<0.01, respectively). Clinical medicine and preventive medicine students were more likely than nursing students to agree that health impacts of climate change are bad (χ^2=20.71, p=0.02) (see Supplemental Material, Table S2).

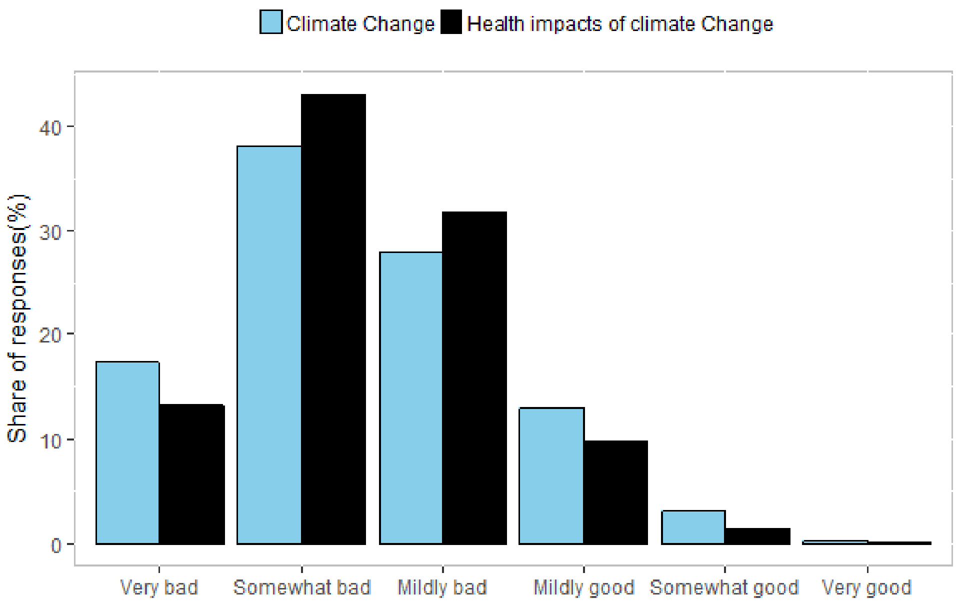


Figure 1. Medical students' perceptions about climate change and its health impacts in general

The average accuracy of all 4 questions about the causes of climate change (true or false) was 57.8%, and the worst knowledge was about global CO_2 concentrations in the atmosphere; only 15.7% students knew about the changes in atmospheric CO_2 concentrations during the past centuries [see Supplemental Material, Table S3]. Only 8.1% of medical students correctly answered all the questions. Nursing student had lower accuracy than clinical medicine and preventive medicine students ($\chi 2=11.32$, $p<0.01$) (see Supplemental Material, Table S4).

In the responses of closed-ended questions about the health impacts and vulnerable groups, over 90% students agreed air quality-related illness, heat-related illness, and disruption of health care services during extreme weather events as expected climate change related health impacts, while fewer identified undernutrition (38.9%) and mental health conditions (63.7%). People who are sick or disabled, seniors, infants or young children, and people living in specific geographic locations were most commonly identified as vulnerable groups. A lower proportion (73%) of respondents identified people with low socioeconomic status as vulnerable (see Supplemental Material, Table S5).

The response rates to the two open-ended questions were both above 85%. The open-ended responses showed some similarities with the closed-ended responses: air quality-related and heat-related illness were the most recognized health impacts of climate change, the vulnerability of seniors, infants or young children, outdoor workers and farmers, people who are sick or disabled and people living in specific geographic locations were also identified by medical students. However, discrepancies were also apparent. Water-borne infectious disease was rarely mentioned on the open-ended responses but identified by over 80% of students in the close-ended question. Respondents ranked vector-borne infectious disease more highly on the open-ended questions than on the closed-ended questions. (Figure 2).

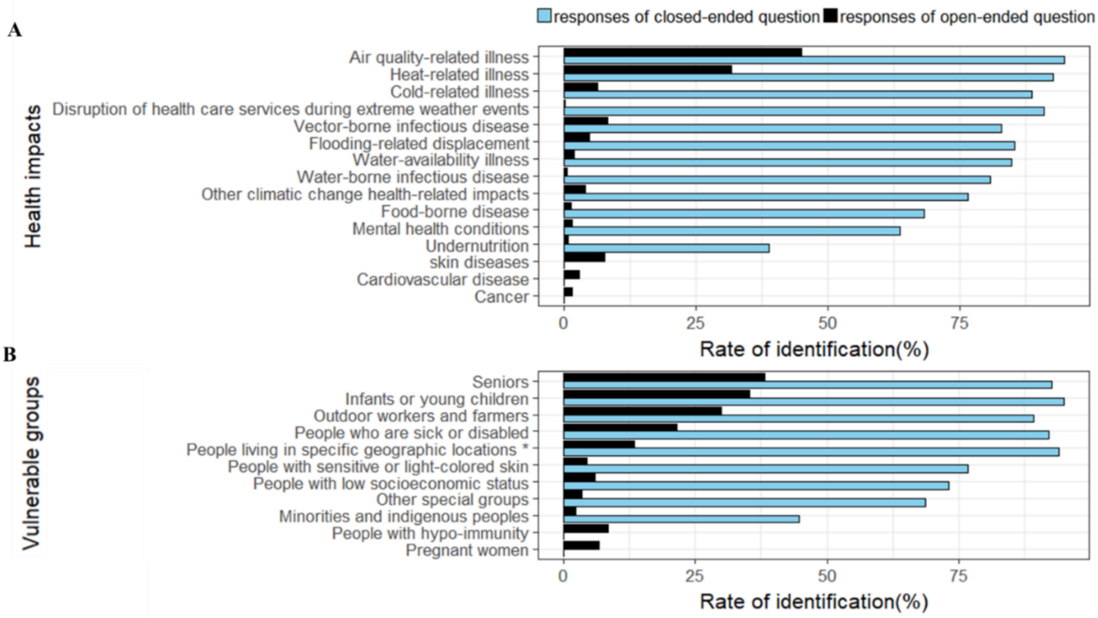


Figure 2. Similarity and discrepancy between open- and closed-ended responses to questions on health-related impacts (A) and vulnerable groups (B) of climate change. *: residents of cities, coastal, storm-prone and flood regions, and other specific regions

Discrepancies of students' perception on health impacts and vulnerable groups existed between different majors (χ^2=12.07, p<0.01, and χ^2=9.23, p<0.01, respectively) (see Supplemental Material, Table S6). And results of logistic regression showed that, compared to clinical medical students, preventive medicine students demonstrated lower awareness of health impacts (OR: 0.71, 95% CI: 0.54, 0.92) and nursing students demonstrated lower awareness of health impacts (OR: 0.69, 95% CI: 0.51, 0.94) and vulnerable groups (OR: 0.59, 95% CI: 0.44, 0.81) (Table 3) .

The majority of students agreed that the climate change health impacts will be serious in the next 20 years, with one third strongly agreeing that the impacts will be serious in China (35.9%) and around the world (39.1%), while a significantly lower percentage (24.6%) noted that it would be serious in their communities. Moreover, preventive medical students were less likely to approve climate change is a local concern (χ^2=22.24, p<0.01) (see Supplemental Material, Table S7). There were also regional differences in this aspect. Students whose hometown located in the western and eastern China were more likely than those who lived in northeastern or central regions to agree that the health impacts would be serious in their communities (χ^2=11.10, p=0.01) (data not shown).

Perceptions of responsibility and ability

Although approximately 90% respondents perceived addressing the health-related impacts of climate change as their responsibility and believed their expertise and skills could play an essential role in doing so, only 50% felt that their expertise and skills are adequate. Similarly, 89.7% medical students agreed that their respective health sector should be concerned about preventing health problems due to climate change, and around 80% believed their sectors' actions would reduce the adverse effects of climate change, yet only 50% believed that health sectors are well-prepared to address climate change-related health impacts (Table 2). Differences of perception on responsibility and ability across the majors were significant (χ^2=18.01, p<0.01) (see Supplemental Material, Table S6). Preventive medicine students had a higher perception of their responsibility and ability than clinical medicine students (OR:1.36, 95% CI: 1.04, 1.78) (Table 3).

Education and training needs

The majority of students thought that they had neither adequate information to respond to current public health emergencies (86%) nor to the potential health risks associated with climate change (87.2%) (data not shown). The most popular information source was the internet (94.5%), followed by electronic mass media (70%) and university teachers (50%). Regarding the authority information sources, Departments of Public Health, Environment Protection Agencies, and Bureaus of Meteorology were most trusted by medical students. Compared to clinical medicine and nursing students, more preventive medicine students identified university teachers as their climate change-related information sources (χ^2=16.9, p<0.01), and more trusted Departments of Public Health (χ^2=19.5, p<0.01). Most respondents (83.1%) reported that staff expertise in climate science is an important resource, followed by technical/analytical skills to assess health impacts (79.7%) (Table 4). The majority of respondents indicated the need for additional information regarding climate change attributable to health risks, and population health/disease tracking database was rated as the most helpful resource (70%) (see Supplemental Material, Table S8).

79.8% of medical students claimed that they did not have the necessary knowledge to address the health-related impacts of climate change. Among these students, 35.8% cited the lack of complete theoretical framework and teachers' guidance as a reason, followed by inadequate training (33.4%), and lack of social and professional attention (19.3%) (data are not shown).

The majority of respondents (especially among preventive medicine students) thought that climate change should be integrated into medical education and training systems. Climate change-related clinical knowledge and skills (71.0%), knowledge of population health (61.6%) and emergency care (59.4%) were identified as the most critical competencies for climate change. Integrating climate change into the medical education curriculum was preferred (32.2%) as the mode for education and training within the current system, while more preventive medicine students (42.6%) preferred specific practical training (Table 5).

Table 2. Medical students' perceptions on their responsibility and ability to address climate change health-related impacts

	Disagree				Agree					
	Total	Strongly disagree	Somewhat disagree	Mildly disagree	Total	Mildly agree	Somewhat agree	Strongly agree	χ^2	*p-value*
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)		
In addressing climate change health-related impacts, medical students themselves……										
Have a responsibility	164 (11.8)	60 (4.3)	59 (4.3)	45 (3.2)	1223 (88.2)	204 (14.7)	473 (34.1)	546 (39.4)		
Can play an important role	154 (11.1)	36 (2.6)	63 (4.5)	56 (4.0)	1232 (88.9)	238 (17.2)	489 (35.3)	505 (36.4)	1116.4	<0.01
Have enough expertise and skills	692 (49.9)	129 (9.3)	237 (17.1)	326 (23.5)	695 (50.2)	357 (25.8)	292 (21.1)	46 (3.3)		
In addressing climate change health-related impacts, the health sectors……										
Should concern about the prevention	143 (10.3)	29 (2.1)	53 (3.8)	61 (4.4)	1243 (89.7)	227 (16.4)	398 (28.7)	618 (44.6)		
Can take effective actions	297 (21.5)	40 (2.9)	109 (7.9)	148 (10.7)	1090 (78.7)	389 (28.1)	456 (32.9)	245 (17.7)	1005.2	<0.01
Are well-prepared	683 (49.3)	118 (8.5)	249 (18.0)	316 (22.8)	703 (50.7)	355 (25.6)	275 (19.8)	73 (5.3)		

Table 3 Factors influencing perception on health impact, vulnerable group, responsibility and ability (N=1,360)

Influence factors	Perception of health impacts		Perception of vulnerable groups		Perception of responsibility and ability	
	OR	95%CI	OR	95%CI	OR	95%CI
Gender						
Male	1	-	1	-	1	-
Female	1.21	(0.94,1.56)	1.27	(0.98, 1.63)	1.16	(0.90, 1.48)
Major						
Clinical medicine	1	-	1	-	1	-
Preventive medicine	0.71*	(0.54, 0.92)	1.09	(0.83, 1.42)	1.36*	(1.04, 1.78)
Nursing	0.69*	(0.51, 0.94)	0.59**	(0.44, 0.81)	0.83	(0.61, 1.12)
Location of hometown						
Central China	1	-	1	-	1	-
Eastern China	0.96	(0.71, 1.29)	1.05	(0.78, 1.41)	1.07	(0.79, 1.44)
Western China	0.90	(0.65, 1.24)	0.86	(0.76, 1.58)	1.03	(0.74, 1.42)
Northeastern China	1.16	(0.80, 1.69)	1.09	(0.62, 1.18)	0.97	(0.67, 1.39)
Per capita income of family						
<$150	1	-	1	-	1	-
$150-299	0.78	(0.52, 1.17)	0.98	(0.65, 1.47)	0.93	(0.61, 1.40)
$300-749	0.99	(0.68, 1.44)	1.08	(0.74, 1.58)	0.84	(0.57, 1.22)
$750-1499	1.07	(0.71, 1.61)-	1.05	(0.70, 1.58)	0.71	(0.47, 1.07)
≥$1500	1.38	(0.84, 2.27)	1.05	(0.65, 1.71)	0.80	(0.49, 1.31)
Self-rated health status					-	-
Very good	1	-	1	-	1	-

Good	0.68**	(0.51, 0.90)	0.85	(0.65, 1.12)	0.87	(0.66, 1.15)
Medium	0.55**	(0.38, 0.80)	0.68*	(0.47, 0.98)	0.60**	(0.42, 0.87)
Poor	0.78	(0.29, 2.10)	0.75	(0.29, 1.95)	0.21**	(0.07, 0.61)

*: p-value<0.05; **: p-value<0.01

Table 4. Medical students' perceptions on information sources and resources (N=1,387)

	Percentage (%)				χ^2	*p-value*
	Total	Clinical medicine	Preventive medicine	Nursing		
Information sources						
Electronic mass media (TV and radio)	70.1	66.6	73.0	73.2	6.9	0.03
Internet	94.5	94.3	94.9	94.6	0.2	0.91
University teacher	50.1	45.5	58.1	48.6	16.9	<0.01
Newspapers/magazines	36.6	35.7	37.9	36.7	0.5	0.76
Friends/neighbors	34.8	37.6	28.4	37.7	11.2	<0.01
Trustful information sources						
Scientists	59.0	60.2	62.1	52.1	8.3	0.02
University/College teachers	33.2	28.4	44.0	28.1	32.7	<0.01
Community health professionals	21.8	22.8	18.6	24.0	3.8	0.15
Departments of Public Health	74.0	69.7	81.6	72.5	19.5	<0.01
Medical communities/associations	43.2	45.5	39.5	43.5	3.8	0.15
Environment Protection Agencies	73.3	70.3	77.4	73.8	6.7	0.04
Bureau of Meteorology	76.4	71.7	79.8	81.2	14.4	<0.01
Non-governmental Organizations	11.9	14.0	11.2	8.6	6.1	0.05
Others	1.5	1.7	1.2	1.6	0.5	0.77
Important resource needs						
Technical/analytical resources to assess health impacts	79.7	77.6	84.9	76.7	10.6	<0.01

Dedicated funding for climate activities	69.3	65.8	74.7	69.0	9.4	<0.01
Staff with expertise in climate sciences	83.1	80.3	87.9	82.1	10.9	<0.01
Technical/analytical resources to assess vulnerability	58.0	55.4	61.9	58.1	4.4	0.11
Better coordination with state agencies	65.1	64.4	70.5	59.1	10.5	<0.01
Better coordination with local agencies	59.1	56.2	65.1	56.9	9.3	<0.01
Others	1.7	1.2	2.1	2.2	1.7	0.43

Table 5. Medical students' perceptions of education and training needs (N=1,387)

	Percentage(%)				χ^2	*p-value*
	Total	Clinical medicine	Preventive medicine	Nursing		
Integrated climate change into medical education systems						
Agree	79.8	71.7	89.1	83.7	51.9	<0.01
Disagree	20.2	28.3	10.9	16.3		
Training needs						
Climate change-related clinical knowledge and skills	71.0	63.8	78.8	75.1	31.5	<0.01
Extended clinical practice	45.6	43.0	47.7	47.9	3.2	0.21
Emergency care	59.4	56.7	59.8	64.5	5.4	0.67
Knowledge of population health	61.6	52.5	75.6	61.0	58.2	<0.01
Knowledge of traditional Chinese medicine	15.9	14.8	15.3	19.2	3.2	0.20
Legal and ethical frameworks	24.8	24.5	25.3	24.6	0.1	0.95
Context in rural and remote practice	28.0	24.4	30.0	32.6	8.3	0.02
Local geographical and climatic knowledge	46.2	39.6	55.6	47.0	26.6	<0.01
Contingency planning and management for extreme weather events	56.3	46.0	67.4	62.3	54.3	<0.01
Others	1.2	1.2	1.6	0.6	1.5	0.48
Preferred training way						
Offer a new independent course	28.7	25.5	27.2	37.4	20.9	<0.01
Integrate climate change into existing medical course	32.2	30.3	35.1	31.9		
Offer specific practical training	31.4	25.9	42.6	27.5		
Others	0.9	0.9	0.7	1.3		

Discussion

As the first nationwide cross-sectional study of climate change and health among medical students in China, this survey helps clarify the level of awareness and the extent of knowledge deficits among the future health workforce in China who will be faced to climate change. Overall, medical students were aware of the health threats posed by climate change and also recognized their responsibility to respond to the problem. At the same time, a striking 50% reported that themselves and the health sector were not well-prepared to tackle climate change-related health threats. Integration of climate change into the existing medical education curriculum would ameliorate information insufficiency and facilitate climate change preparedness.

Knowledge and Perceptions

Most medical students in China were aware of the threats of climate change and its health impacts. This was consistent with findings from previous studies conducted in public health officers in California [14], American public health nurses [16], African American physicians [19], and health science students in Ethiopia [20]. This high awareness can be served as a good start point for preparing and engaging medical students to tackle climate change.

Female students had a marginally better understanding of the harmfulness of climate change than the males, similar to studies in Ethiopia [20] and Malaysia [21]. The explanation may be that females hold more scientifically accurate beliefs about climate change than males do [22]; it may also be that social concerns like the impact of climate change and health are somewhat gendered via socialization and other norms.

Despite widespread concern and relatively high awareness, important misunderstandings were evident that climate change is perceived by some of the medical students as a distant threat with limited personal relevance. Previous surveys to public health nurses [16] and environmental health directors [23] also showed that, compared to the United States and around the world, fewer health professionals believed the impacts would be greater in their jurisdiction. Since climate change impacts exhibit large geographic variations, local conditions must be taken into consideration while tackling climate change. This kind of underestimation toward local threats could limit their motivation linking climate change with locally observed health effects. Incorporating downscaled, locally relevant projections of climate change and the ranges of likely health effects might be a useful approach to this concern.

Respondents who lived in the west and east regions of China were more likely than other regions to believe that climate change is a local community concern. These differences may stem from personal experiences caused by different levels of exposures, as well as unmeasured social, cultural, or economic factors. Several studies suggest that personal experience is a significant determinant of people's awareness of climate change [24-26]. Limited socioeconomic development in the western region might cause limited adaptation, and the eastern region is exposed to more heat extreme and other extreme weather events, suggesting that people living in these regions may have more direct experiences of extreme weather and climate hazards and thus are more likely to recognize climate change as a local concern.

The present study indicated that Chinese medical students were lack of specific knowledge on atmospheric CO2 concentrations. According to a cross-country study in 2016 [27], knowledge of the causal drivers of climate change was correlated with higher levels of concern about climate change because it clarifies linkages between specific activities and greenhouse gas levels. Thus, there is a clear need to better inform medical students about the mechanisms and drivers of climate change.

The responses of closed-ended questions suggested that students may recognize the direct impacts of climate change on health but were likely to ignore more indirect pathways. Specifically, the identification of respiratory disease was larger than in any previous studies [16, 23, 28]. One possible reason is that air pollution in China has worsened in recent years, which has aroused widespread media attention and became one of the most important environmental crises now [29]. And heat-related illness was identified to be a climate threat by the majority of respondents in our study, consistent with several previous studies [14, 19, 28], while smaller percentages were reported by public health officers in Oregon [30], public health nurses [16], health science students in Ethiopia [20]. The differential findings may be due to different levels of heat exposure at the different locality.

On the other hand, mental health impacts were the least frequently identified as climate change-related health concern in our study, similar to local health department directors [28] and public health officers in Oregon [30], though a higher concern was shown by public health nurses [16]. This may reflect a general bias toward under-recognition of the substantial mental health disease burden or be part of the trend toward a heightened awareness of direct climate-health effects observed among Chinese students. Even though undernutrition has been widely recognized as an important climate change-related health impact, a relatively low proportion of respondents identified it as a significant concern in our study. As undernutrition is heavily mediated through human institutions, people may underestimate this indirect impact of climate change. However, undernutrition could be a more pressing concern in the future, as China's large population and low per-capita resources may bring more challenges related to food insecurity driven by climate change [31].

From the discrepancy between closed-ended and open-ended responses, we argued that people's unprompted responses to our open-ended questions are likely a reflection of their actual understanding of the effects of climate change on health than their responses to close-ended questions. Because the responses to close-ended questions may be subject to three kinds of bias as following. First, respondents' answers to close-ended questions may reflect prompted recall, but with an open-ended question, the information was not available to them in an unaided memory search. Second, respondents who have relatively firm beliefs about the reality/unreality of climate change may tend to accept/deny all answers, which is harder for them to do with open-ended questions. Third, respondents who do not hold firm opinions on the reality and harmfulness of climate change may have an easier time inferring the "right" answers (the answers they think the investigators want to hear) and providing those answers in response to close-ended questions [15]. Fewer concerns were articulated overall in open-ended responses than in questions with closed-ended prompts, suggesting that students may recognize the myriad ways in which climate change can affect health but be less confident of which relationships to climate change as particularly significant. Therefore, education efforts in information dissemination are needed, and additional emphasis needs to be placed on indirect causal pathways through which climate change can affect our health.

Preparedness

Medical students in our study strongly endorsed their role in responding to climate change and its health impacts. This high sense of professional responsibility implies favourable conditions for engaging them in climate and health education, advocacy campaigns or even broader environmental health issues. However, a large proportion of students did not believe that themselves or the health sector had made adequate preparations to climate change. Many public health officers in the USA also claimed their departments are having insufficient knowledge, expertise and capacity [16, 28, 30] and this situation are thought to be even worse in China. The gap between responsibility and ability should raise the concern about what capabilities are necessary for health professionals in the context of climate change and what institutional settings can make health sectors more resilient to climate change.

Medical education

The need for additional resources to address climate change was acknowledged by many medical students. Experts on climate change and health were identified as the most pressing need in our study, while lack of funding was the greatest concern among public health officers in the USA [14, 28, 30]. This suggests different barriers to implementing climate adaptation measures in different countries. To better cope with climate change, China should increase the cultivation and reserve of interdisciplinary talents for climate change and health.

Internet and other electronic mass media (TV and radio) were demonstrated as the most popular source of information on climate change among our respondents, similar to previous studies in Ethiopia [20] and in Malaysia [21], while nine tenths of local public health officers in California chose scientists as their information source [14]. Our finding highlights the critical role of mass media in covering climate change and in helping guide climate change-related education and communication efforts. Further studies on the role of the internet and social media may facilitate the development of strategies to increase students' knowledge of climate change impacts. This finding also suggests there may be an informational vacuum in medical student training, and there is a need for explicit treatment of the topic in the Chinese medical curriculum.

Based on our results, Chinese medical students still need many improvements in their perception and preparedness, and we argue against addressing this issue through educational efforts. In response to climate change, a qualified health professional should be able to obtain, understand, integrate and employ climate change and health-related ecological effects information and improve health services. This kind of ability was defined by Bell [32] as "eco-medical literacy". Developing eco-medical literacy and capacity building among medical students can help facilitate preparedness. Maxwell and Blashki [33] argued that curriculum integration is the most straightforward and efficient approach with this aim, and this approach was also widely suggested by our respondents. Relevant courses on the climate change/human health interface could be included in the curriculum of Chinese universities, and expanded medical curriculum should be first carried out among preventive medicine students given their lower perception of climate change and its health impacts. These efforts can leverage activities to promote climate and health education already underway through the Global Consortium on Climate and Health Education, an initiative funded by The Rockefeller Foundation, which aims to unite schools of medicine, nursing and public health in sharing best practices to build curricula and core training [7]. Chinese medical universities may join this consortium, and follow-up studies may comprehensively reveal what competencies are needed and what educational modes are appropriate to achieve satisfactory knowledge of medical students at graduation.

Some limitations of this study should be considered. First, although our sampling frame was designed to gather opinions from a range of a region in China, not all results could be generalized to the overall cohort of Chinese medical students. Because the students engaged in this study were from top universities in China, there may be a lower perception in other universities. Second, as data on personal extreme weather experience were not collected, we cannot explore it as a potential driver for the regional difference of perceptions. Third, this is an opinion survey, and there are no gold standards for most questions. However, we think it is still valuable to understand the current students' perceptions of climate change, both in terms of overall perceptions of health risks and vulnerability, and in providing meaningful information of perception and information deficits.

Conclusions

Most medical students in China were aware of climate change and its health impacts. Although medical students embraced their role in responding to climate change, they did not feel that themselves or the health sector are adequately prepared. The high awareness and level of concern, in general, can serve as a strong foundation for developing additional training in medical education, and particularly efforts should be considered to integrate climate change into established curricula.

References

1. Smith, K. R.; Woodward, A.; Campbell-Lendrum, D.; Chadee, D. D.; Honda, Y.; Liu, Q.; Olwoch, J. M.; Revich, B.; Sauerborn, R., Human health: impacts, adaptation, and co-benefits. In: Climate Change 2014: Impacts, Adaptation, and Vulnerability. Part A: Global and Sectoral Aspects. Contribution of Working Group II to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change. Cambridge University Press, Cambridge, United Kingdom and New York, NY, USA 2014, 709-754.
2. Watts, N.; Adger, W. N.; Agnolucci, P.; Blackstock, J.; Byass, P.; Cai, W.; Chaytor, S.; Colbourn, T.; Collins, M.; Cooper, A.; Cox, P. M.; Depledge, J.; Drummond, P.; Ekins, P.; Galaz, V.; Grace, D.; Graham, H.; Grubb, M.; Haines, A.; Hamilton, I.; Hunter, A.; Jiang, X.; Li, M.; Kelman, I.; Liang, L.; Lott, M.; Lowe, R.; Luo, Y.; Mace, G.; Maslin, M.; Nilsson, M.; Oreszczyn, T.; Pye, S.; Quinn, T.; Svensdotter, M.; Venevsky, S.; Warner, K.; Xu, B.; Yang, J.; Yin, Y.; Yu, C.; Zhang, Q.; Gong, P.; Montgomery, H.; Costello, A., Health and climate change: policy responses to protect public health. *Lancet* **2015**, 386, (10006), 1861-914.
3. Zing, N.; Ding, Y.; Pan, J.; Wang, H.; Gregg, J., Climate change-the Chinese challenge. Science-New York Then Washington- 2008, 319, (5864), 730.
4. McMichael, T.; Montgomery, H.; Costello, A., Health risks, present and future, from global climate change. *Bmj* **2012**, 344, e1359.
5. Haines, A.; Ebi, K. L.; Smith, K. R.; Woodward, A., Health risks of climate change: act now or pay later. *Lancet* **2014**, 384, (9948), 1073-5.
6. Who, Protecting health from climate change: World Health Day 2008. In 2008.
7. Friedrich, M. J., Medical Community Gathers Steam to Tackle Climate's Health Effects. *Jama* **2017**, 317, (15), 1511-1513.
8. Gill, M., Why should doctors be interested in climate change? *Bmj* **2008**, 336, (7659), 1506.
9. Gill, M.; Stott, R., Health professionals must act to tackle climate change. *Lancet* **2009**, 374, (9706), 1953-5.
10. Green, E. I.; Blashki, G.; Berry, H. L.; Harley, D.; Horton, G.; Hall, G., Preparing Australian medical students for climate change. *Aust Fam Physician* **2009**, 38, (9), 726-9.
11. McMichael, A. J.; Friel, S.; Nyong, A.; Corvalan, C., Global environmental change and health: impacts, inequalities, and the health sector. *BMJ* **2008**, 336, (7637), 191-194.
12. Weaver, H. J.; Blashki, G. A.; Capon, A. G.; McMichael, A. J., Climate change and Australia's healthcare system - risks, research and responses. Aust Health Rev 2010, 34, (4), 441-4.
13. Maibach, E. W.; Chadwick, A.; McBride, D.; Chuk, M.; Ebi, K. L.; Balbus, J., Climate Change and Local Public Health in the United States: Preparedness, Programs and Perceptions of Local Public Health Department Directors. PLoS ONE 2008, 3, (7), e2838.
14. Bedsworth, L., Preparing for climate change: a perspective from local public health officers in California. Environ Health Perspect 2009, 117, (4), 617-23.
15. Maibach, E. W.; Kreslake, J. M.; Roser-Renouf, C.; Rosenthal, S.; Feinberg, G.; Leiserowitz, A. A., Do Americans Understand That Global Warming Is Harmful to Human Health? Evidence From a National Survey. Ann Glob Health 2015, 81, (3), 396-409.
16. Polivka, B. J.; Chaudry, R. V.; Mac, C. J., Public health nurses' knowledge and attitudes regarding climate change. Environ Health Perspect 2012, 120, (3), 321-5.
17. Roser-Renouf, C.; Maibach, E. W.; Li, J., Adapting to the Changing Climate: An Assessment of Local Health Department Preparations for Climate Change-Related Health Threats, 2008-2012. PLoS One 2016, 11, (3), e0151558.
18. National Bureau of Statistics of, C., Partitioning method of east, central, west and northeast region in mainland China. In 2011.

Chapter 3. Public health adaptation to extreme heat events in response to climate change in the Asia-Pacific Region

Yiling HE[1], Rui MA[1], Meng REN[1], Wenmin LIAO[1], Na ZHANG[1], Yanan SU[1], Cho Kwong Charlie LAM[2], Suhan WANG[1], Cunrui HUANG[1,*]

[1] School of Public Health, Sun Yat-sen University, 74 Zhongshan 2nd Road, Yuexiu District, Guangzhou 510080, Guangdong Province, China
[2] School of Atmospheric Sciences, Sun Yat-sen University, 135 Xingang Xi Road, Haizhu District, Guangzhou, Guangdong Province, China
[*] Correspondence: huangcr@mail.sysu.edu.cn, School of Public Health, Sun Yat-sen University, Zhongshan Road #2, Guangzhou 510080, China (C.H.)

Abstract: This chapter examines heat-related health effects and suggests public health adaptation strategies to extreme heat events in the Asia-Pacific region. Due to climate change and urban heat island effects, a future increase in heat waves could lead to excess heat-related mortality and morbidity among vulnerable populations. However, the risk of heat exposure is not evenly distributed. Some demographic groups are more prone to heat-related illnesses, such as outdoor workers, children, the elderly and people with pre-existing health conditions. Furthermore, population ageing and acclimatization limits both present challenges for adapting to a warmer climate. Considering these challenges, this chapter identifies several adaptation strategies to address the health impacts of heat waves and discusses the issues of implementing these policies and measures. For example, heat-health action plans require the government to coordinate with supporting agencies for deciding the timing of activation and deactivation. Heat-health warning systems can also be developed based on temperature threshold, but this threshold varies in different cities. During heat waves, real-time surveillance data can provide early detection of heat-related health threats. In addition, the government can use heat vulnerability mapping to identify populations susceptible to heat waves and provide adequate healthcare and social services for these vulnerable groups. Identifying vulnerable populations alone is insufficient, as effective risk communication is required for behaviour change, including personal heat exposure reduction strategies. Finally, climate-sensitive urban planning such as optimizing building design and urban greening would alleviate the adverse health impacts of heat waves.

Keywords: heat wave; climate change; health impact; vulnerability; adaptation strategy; China

Introduction

Countries worldwide have experienced numerous extreme heat events in the early 21st century, such as Europe in 2003, Russia in 2010, and Southeast Asia in 2016 [1]. These events were associated with increased rates of mortality and morbidity, with higher risks among vulnerable groups including outdoor labours, children, the elderly, and people with pre-existing chronic diseases.

Most of the adverse health effects of hot weather are preventable, which can be achieved by appropriate and effective public health response, including strategies for short-term measures, medium-term preparedness and long-term plans. In this chapter, we aim to reflect our collaborative work on epidemiological evidence about temperature-related health effects in the Asia-Pacific region, draw attention to population susceptibility to temperature extremes, as well as the development of public health adaptation strategies to cope with problems associated with current and future heat waves.

Defining the problem

Heat waves can cause a wide range of health problems (Figure 1), and the effects are modified by other meteorological and sociodemographic factors. As the front line of medical service, ambulance dispatches include a comprehensive array of health conditions in the population scale. Using a large dataset of ambulance dispatches, He et al. [2] found a significantly rising risk of ambulance dispatches during heat events in Shenzhen, China. Wider range of heat-related diseases was reported compared with mortality or hospitalization data; they were urinary disease, alcohol intoxication, obstetric and gynaecological disease, dizziness, respiratory disease, traumatic disease, and gastrointestinal disease. Bao et al. [3] revealed that high temperatures in hot months might trigger first-ever strokes, and low atmospheric pressure may exacerbate the effect in Shenzhen, China. Also, Wang et al. [4] found interaction effects of air temperature and humidity in Guangzhou, China, on the relationship between PM10 exposure and small for gestational age among newborns conceived in the warm season (May–October). Liu et al. [5] conducted a comprehensive study to quantify the heat-related years of life lost (YLLs) of future warming climate under the RCP scenarios on a local scale in China. Results revealed that heat effects might increase dramatically with continued rapid population expansion processes and population ageing in the future.

Research in other parts of Asia also found the significantly rising risks of mortality and morbidity during heat events. For example, Dang et al. [6]examined the effects of extreme heat events on mortality and hospitalization in Ho Chi Minh City, the most populous city of Vietnam. The effect of heat waves significantly increased the risk of all cause-specific mortality and hospitalization for respiratory diseases. Phung et al. [7] examined spatial variability of heat-related morbidity in multiple districts of the Mekong Delta Region, Vietnam. Heterogeneous of temperature-hospitalization risks were found across districts. Population density, percent of females, pre-school students and rural population in districts could lead to this heterogeneity. In Thailand, Huang et al. [8] found that the highest risks of deaths during heat waves were from certain infectious and parasitic diseases and neoplasms, causing considerable mortality burden. Northern and Central Thailand were the regions more vulnerable to heat waves, and the proportion of the elderly population was the primary driver behind the spatial heterogeneity of heat vulnerability.

Heat can also pose threats to occupational health. Sheng et al. [9] found a higher risk of work-related injuries due to hot weather in Guangzhou, China. Significant associations were seen for both males and females, and middle-aged workers. At risk, occupations included manufacturing, transport and construction sectors. Using the same dataset, Ma et al. [10] further revealed that heat stress could contribute to not an only higher risk of work injury but also substantial economic costs. 4.8% (95% eCI: 2.9%–6.9%) of work-related injuries and 4.1% (95% eCI: 0.2%–7.7%) of work-related injury insurance payouts were attributed to heat exposure. More frequent and higher risks were found for minor injuries. Workers with low educational attainment and working in small enterprises were sensitive to the effects of heat exposure.

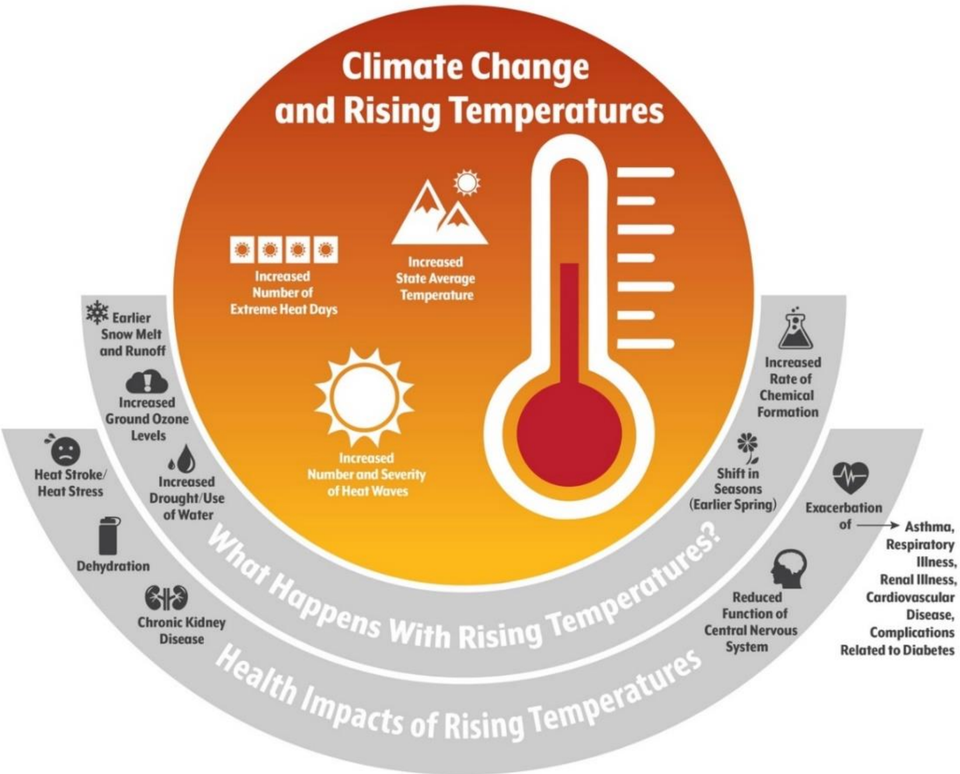


Figure 1. Rising temperature and its health impacts. Source: [11].

In summary, the exposure-response relationship between temperature and mortality or morbidity is usually found to be U-, V- or J-shaped, with increasing risk at the upper end of the temperature scale [12]. However, the impacts of heat waves may be not restricted to the period in which the event occurs which shows a lag effect ranging from the same day to 3 days [12, 13]. Moreover, the interactions between air pollution and extreme temperatures on health should not be ignored in many cases.

Air pollutants such as particulate matters, ozone and carbon monoxide are often associated with increased mortality at high temperatures, usually causing cardiovascular and cardiopulmonary diseases and also the impact varies across regions [14]. In general, the adverse health effects are location-specific and seem to change over time as well [15]. Therefore, systematic collection and tracking of health outcomes are important for both assessing heat-related health effects among vulnerable groups and monitoring heat adaptation over time.

Understanding susceptibility

As heat exposure usually is perceptible, it is relatively easy for exposed individuals to escape from thermal environments. However, individual behaviour or ability in coping with heat events are often influenced by socioeconomic, behavioural, cultural, and other factors. Our research and recent studies have identified multiple vulnerable subgroups, including outdoor workers, children, the elderly, people with pre-existing diseases, urban residents, and those with low socioeconomic status [16].

Outdoor workers

Outdoor workers are especially vulnerable because they are easy to accumulate excessive heat in the body during daytime extremes. Heat accumulation mainly roots in external heat exposure (high air temperature and solar radiation) and internal metabolic heat production due to heavy physical labours [17]. Required personal protective equipment may also increase workers' thermal storage. Furthermore, outdoor workers may be exposed to extra occupational hazards (like exhaust fumes, hot asphalt and pesticides) [18]. Agriculture and construction are the most severely influenced outdoor sectors, but groundskeepers, transportation and mining workers are also reported at the high risk of occupational heat-related health effects [19, 20].

Children and the elderly

Children are sensitive to heat because of their developing organs and nervous systems, immature cognition, rapid metabolisms, limited experience and behavioural characteristics [21]. Studies have found that children aged under 5 were at a significantly higher risk for heat stroke when playing outdoors because they are usually less equipped on many fronts to deal with heat stress and may lack appreciation about heat-related illnesses [22]. The vulnerability of older people mainly due to the degeneration of the thermoregulatory system, the increase of co-morbidities, as well as medications use [23]. During the 2003 heat waves in Paris, the elderly over 75 accounted for >80% of the total excessive death [24]. However, many senior people were less tend to take protective measures during heat waves because of the under-appreciation of their vulnerability [25].

Pre-existing diseases

Cooling is usually achieved physiologically by increasing skin blood flow and sweating. The condition of the cardiovascular system as well as the endocrine, urinary and integumentary systems will influence the heat dissipation progress [26]. Therefore, people with specific diseases which compromise the cooling mechanisms may be more susceptible to heat (e.g., cardiovascular and cerebrovascular diseases, renal diseases, respiratory diseases, diabetes, and mental disorders) [27-29]. Some medications used to treat physical and mental illnesses, such as prescribed antipsychotics, antidepressants, and antihypertensive drugs, may reduce the sensory perception of surrounding heat or inhibit thermoregulation. For example, thirsting and sweating progress can be compromised [30, 31]. Thus patients taking these medications are at a higher risk during heat waves [32].

Urban residents

Urban residents now comprise over half of the world's population. The temperature difference between urban regions and the surrounding rural areas ranged from 1 °C to 6 °C [33]. The reliable explanations on "urban heat island effects" include high thermal absorption in daytime and heat emission at night by pavements and buildings, lack of green space, and reduced airflow around high crowed buildings [29, 34-36]. With the rapid urbanization and population migration in China, more people are swarming into big coastal and southern cities. People used to live in cooler northern China may not adapt to the hot and wet climates in Southern China [37].

Moreover, people from cooler regions are usually not well acclimated and less likely to use air-conditioner, which could contribute to greater heat-related mortality and morbidity [38]. Research has also shown that the minimum temperatures for fatal heat-related illnesses decrease with increasing latitudes [39]. The differences between physiologic and technologic adaptations adopted by residents could result in various health event thresholds [38].

Socioeconomic factors

Income was associated with heat-related mortality at the neighbourhood level in Hong Kong, China [40]. The plausible underlying explanation may include: a) low-income individuals are less willing to respond to heat warnings or pay for transportation to cooler locations [41]; b) low prevalence of air conditioning, lack of medical care, and health insurance shortage [29, 41]; and c) housing characteristics. Well-insulated homes were reported to have a protective effect against heat-related mortality, whereas individuals in older buildings with poor thermal insulation function were at a higher risk [42].

During the 2003 heat wave in Europe, higher education was reported as a protective factor of heat-related illnesses [43]. The composition of neighbourhood education was related to heat-associated mortality, whereas the results were mixed when considering education effects at the community level [44]. Other factors which are related to educational levels, such as income inequality, the distinction of occupations, or perception of heat events, may also affect the risk of heat-related illnesses.

Social isolation is usually reported as a risk factor in heat-related illnesses. People at higher risk typically have limited association with their relatives, neighbours, or social services (like unmarried or widowed, living alone, the elderly, the poor and homeless, and physically disabled) [45]. Social isolation may be a consequence of physical, mental, or cognitive damage according to existing studies [34].

Summary indicators of socioeconomic status have also been applied to explore the vulnerable populations in heat waves. Summary indicators may have advantages in modelling the latent class represented by the combination of individual factors, and it is statistically advantageous when the components are strongly associated. However, the summary measure does not provide information concerning the individual effects of income or education on vulnerability [40].

Future Drivers

Climate change

Base on the observations worldwide, the IPCC has concluded that climate change has happened on a global scale. Though the Paris Agreement has set goals of limiting the warming within 2 °C and call on efforts on limiting temperature rise within 1.5 °C above pre-industrial levels, we will still face deteriorated heat wave exposure with increasing intensity and frequency. According to Dosio et al. [46], in a 1.5 °, C warming world most regions at low latitudes will be affected by severe heat events, but the frequency of these events will even double with a 2 °C warming compared with 1.5 °C warming (Figure 2). As for the affected people, 13.8% of the world's population will be frequently exposed to severe heat events at a 1.5 °C warming, while the number will triple with a 2 °C warming.

Dynamical downscaling of a global climate model was applied at a 60-km horizontal resolution to project temperature changes from 1990–1999 to 2045–2054 over Southeast Asia [47]. Projected warming varies from < 0.1 to 3 °C depending on the location and season, with greater warming at night than daytime for all seasons. Figure 3 shows changes in the annual and seasonal means of daily maximum temperatures from the 1990s to 2050s. Results show the simulated changes in annual mean Tmax (Figure 3(a)) range between 0.5 and 1.0 °C over the northern and central part of the domain, including most parts of Thailand, Burma, Laos and northern Vietnam. Larger changes in Tmax (1.0–1.5 °C) are simulated over the southern part of the domain, including Cambodia, Southern Vietnam, southern Thailand and Island countries.

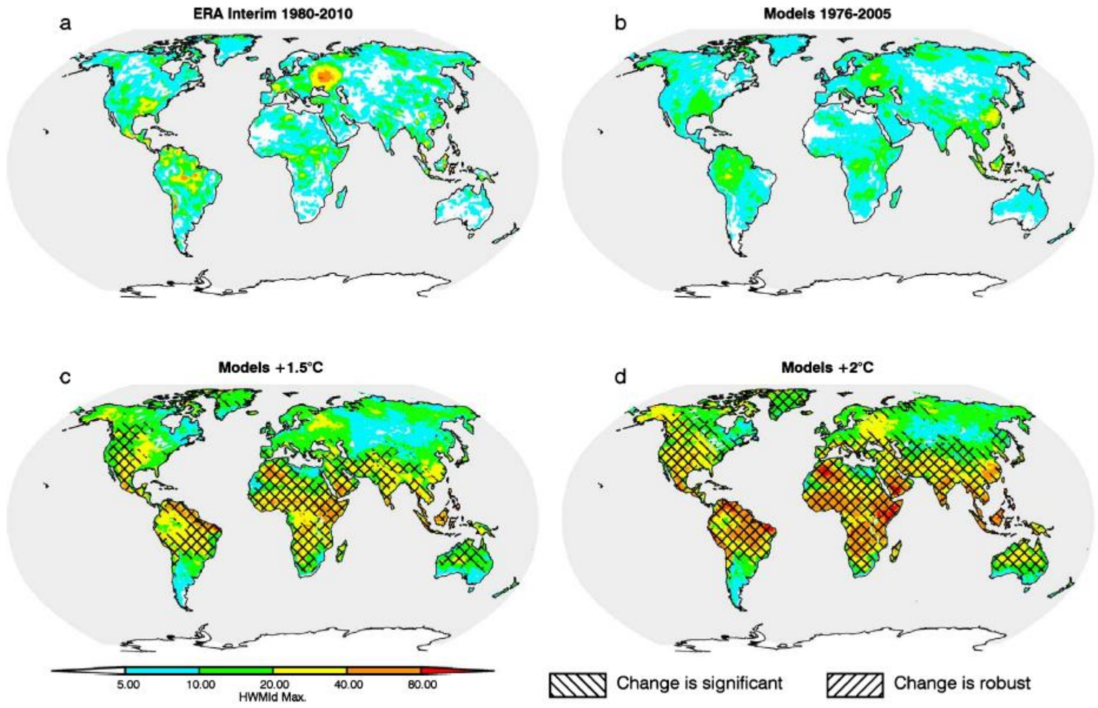


Figure 2. Present and future distribution of heat waves. (a) Maximum heat wave magnitude observed during 1980–2010. (b) Modelled maximum magnitude during 1976–2005. (c) Projected maximum magnitude in a 1.5 °C warming world, and (d) a 2 °C warming world. Source: [46].

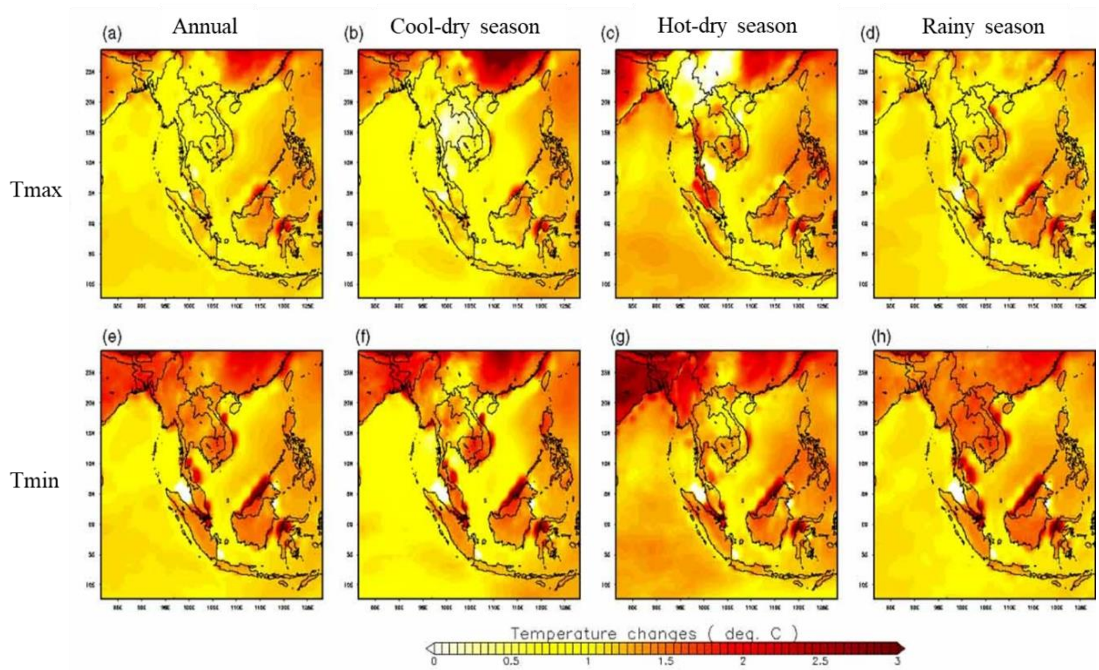


Figure 3. Changes of the 2050s daily average Weather Research and Forecasting (WRF) model simulated for annual Tmax (a), cool–dry season Tmax (b), hot–dry season Tmax (c) rainy season Tmax (d), annual Tmin (e), cool–dry season Tmin (f), hot–dry season Tmin (g), rainy season Tmax (h). Source: [47].

Rapid urbanization

There is about 54.7% of the population living in urban areas globally in 2018, and this figure will reach 68.4% by 2050 [48]. The rapid urbanization has influenced our environment profoundly. Buildings absorb more solar radiation; greenhouse effect reduces heat escaping into space; these make urban areas warmer than surrounding areas. The extra heat could exacerbate the health impacts of heat waves. A study in the UK found that urban heat islands (UHI) contributed half of the heat-related deaths, and health impact assessments ignoring the regional difference of temperature resulted in a 20% underestimation in mortality [49].

Despite being less urbanized than most other regions today, Asia is home to 54 % of the world's urban population [48]. While Southeast Asia is one of the world's least urbanized regions, its rate of urban population is growing unprecedently, 1.72 times faster than the world's rate[48]. Figure 4 shows the urbanization of Asia. Eastern Asia region shows a higher rate of urbanization than that in other parts of Asia. The urban proportion may rise beyond 60 percent by 2050s. Human settlements and the influence of human activities and city development have expanded with urbanization. On a local basis, these factors have the potential to increase the vulnerability of ecosystems and communities to climate change. The continuous growth of urban residents may increase the exposed population and present a severe challenge to health sectors.

a. b.

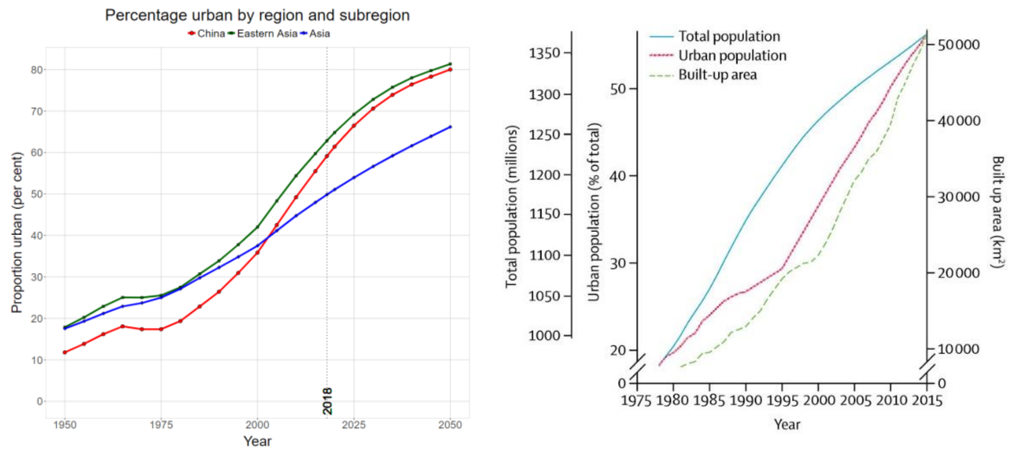


Figure 4. Urbanization in China, Eastern Asia and the Asia. a) Percentage urban in China, Eastern Asia and the Asia, 1950-2050s (Source: [48]); b) Total population, urban population and built-up area in China, 1978-2015 (Adapted from: [50]).

Note: Proportion of urban population in China as compared to its subregion and region. The proportion is expressed as a percentage of the total population, 1950 to 2050.

Population ageing

Population ageing is the case for most countries. Advanced age represents one of the most significant risk factors for heat-related health effects. The elderly usually have diminished physiological heat adaptation ability due to poorer thermoregulation and suffer from underlying diseases, such as coronary heart disease and chronic lung disease. The elderly are more likely to live alone and have reduced social contacts. Therefore, the social and physiological vulnerabilities to heat waves will increase greatly because of a larger proportion of the elderly in the near future.

The Asia-Pacific region is going through profound and rapid population change. Countries in Asia and the Pacific are in the process of ageing at an unprecedented pace. In 2018, approximately 13% of the population in this region are over 60 years old, and this figure is projected to nearly reaching a quarter, achieving around 1.3 billion people by 2050 [51]. Figure 5 shows the estimates and projections of populations by age and gender in Asia.

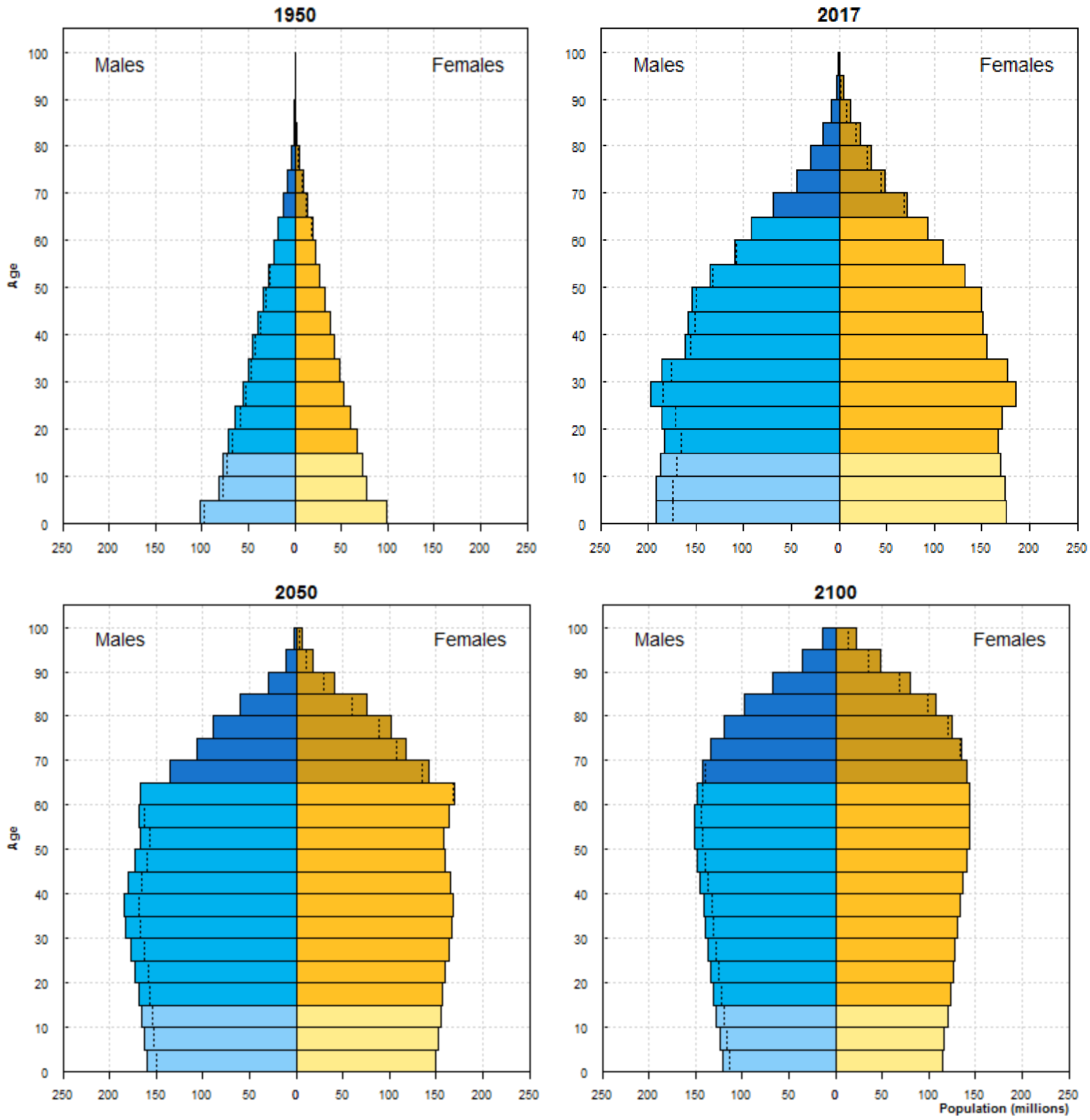


Figure 5. Population by Age and Gender in Asia in 1950, 2017, 2050 and 2100. The dotted line indicates the excess male or female population in certain age groups. The data are in thousands or millions and represent the population in each age group. Source: [52]

Acclimatization limits

Considering that humans have already tolerated a wide range of climate, many people are optimistic that human will simply adapt to future, increasing temperature. Previous studies indicated that heat-related mortality varied among different regions [53]. It usually attributes to behavioural and technological adaptation as well as physiological acclimatization. Taking the time horizon into consideration, it has aroused intense discussion in academia if humans can acclimatize to future increased heat exposures due to climate change.

Sherwood and Huber [54] concluded that when global mean temperature increases by 7 °C, metabolic heat dissipation will become impossible in some regions due to the human limits to heat tolerance. When the mean global temperature increases by about 11-12 °C, these regions would expand to encompass most of today's human habitation, since it becomes challenging to dissipate metabolic heat, it would induce hyperthermia in humans and other warm-blooded animals when body temperature exceeds 35 °C for extended periods. Sherwood and Huber [54] pay much attention to the variation of mean temperature conditions and the relevant variation of maximum temperatures distribution during a few centuries. They found that, though the variation of mean global temperature is little, it is more likely to exceed physiologically tolerable thermal limits when the mean temperature is higher. If the mean global temperature increases above 4-6 °C, human biology may be physiologically maladaptive to the new thermal environment.

From an evolutionary perspective, biological evolution is a long process. Fossil records indicate that the slow undulatory processes of global cooling during the past 65 million years has led to the increased body size of warm-blooded mammalian. Thus, they could reduce heat dissipation to the external environment. During the evolution of nanoseconds over the next few centuries, it would be impossible for human mammals to go through useful genetic acclimatization. There is no denying that the population has experienced an exponential increase from millions to billions. When gene pool is larger, it is faster to respond to the variation in environment and interbreeding between regional genetic strains will increase. Nevertheless, many scientists warned that it would not be possible for a biological evolutionary adaptation to a warmer climate in a few hundred years [55].

Apart from the perspective of physiology or evolution, a hotter world will not only be less livable, but it will also reduce productivity, which will become an obstacle to acclimatization in return. It is due to the interruption of the production process in nature that we rely on, and because of the impaired work capacity in overheated conditions [56]. Zander et al. (2015) analyzed estimates of job absences and performance degradation of about 2,000 workers resulting from heat during 2013–2014 in Australia [57]. Around 75% of respondents said that heat exposure in the workplace had affected their work efficiency. The authors then conducted further research and found that the cost for one person was about annual 655 U.S. dollars. Through speculation, this study shows that the cost for the Australian economy is about 6.2 billion U.S. dollars (accounted for 0.4% of GDP in 2014). Until now, however, many governments have not fully realized that heat exposure had a profound impact on workability and economy productivity, nor take them into consideration of future projections and plans for social and economic development [58].

Public health response and adaptation strategies

Public health adaptation aims to reduce undesirable health impacts or enhance resilience to heat waves through short- and long-term actions [59]. However, adaptation strategies may fall into autonomous and planned actions [60]. Although autonomous adaptations can occur without coordinated scheming in individual or community levels and are usually reactive by nature, well-planned adaptations will involve deliberate policy actions with conscious intervention basing on anticipated risks. Thus, planning is more important for public health communities to cope with the adverse effects of heat waves.

Adaptation policies

Many government authorities have developed multiagency and intersectoral policies or regulations in response to heat events. Among these policies, heat-health action plans (HAPs) are core policy elements in public health adaptation to heat waves. Developing an effective HAP requires a lead agency which coordinates with all participating or supporting agencies, sets criteria to determine the threshold for HAP's activation and deactivation in the city-specific setting. This lead agency also sets a risk communication and public education plan to deliver heat-related health information, detects high-risk populations, and determines ways to reach most vulnerable groups [61, 62].

Developing and participating HAPs among agencies and the public could help decrease adverse health impacts of heat and heat-related mortality [63-65]. For example, public health authorities in Montreal city of Canada developed heat-health action plans in 2004, which would be activated when forecast temperatures are exceeding 30°C (86°F). After a revision in 2012, the current Montreal Heat Response Plan (MHRP) comprises five levels, which including Normal, Seasonal watch, Active watch, Alert and Intervention (Figure 6). Different actions such as public advisories, risk information transmission, intensified surveillance and air-conditioned shelters opening will be taken depended on different alert levels [66]. Benmarhnia et al. [67] reported that the actions of MHRP had been proved effective in reducing heat-related mortality by 2.5 deaths per day when extreme heat occurred.

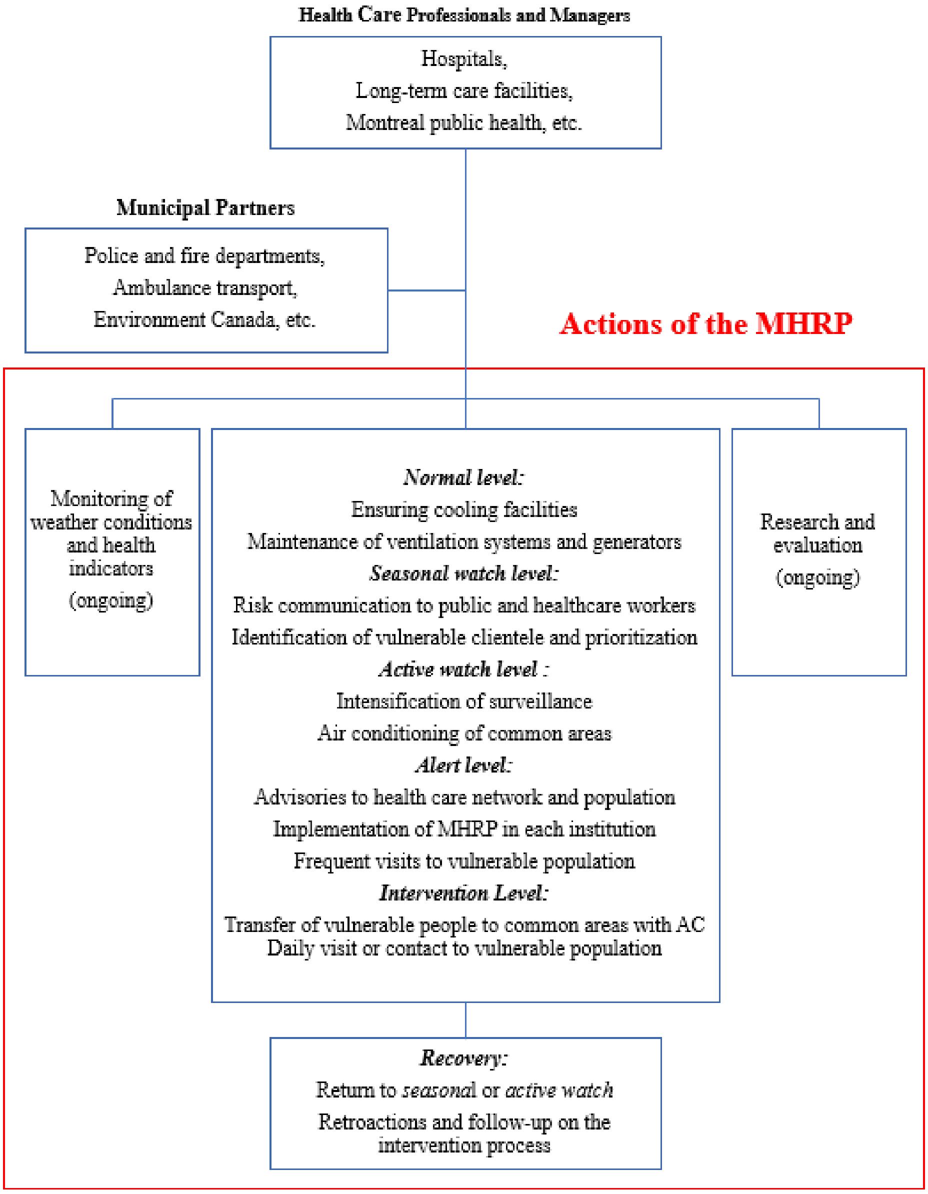


Figure 6. Logic model for the Montreal Heat Response Plan (MHRP). Adapted from: [68].

In 2012, the Chinese state government released The Administrative Measures on Heatstroke Prevention (AMHP2012) to address intense heat events. Some critical countermeasures in this regulation include applying new materials and technologies, constructing protective equipment, monitoring and examining the health status of labours. In addition, this regulation requires employers to adjust shift time by weather forecasting and pay high-temperature subsidies to workers during hot days. More importantly, once diagnosed as an occupational disease due to occupational heat exposure, labours have every right to enjoy the treatments of industrial injury insurance regulations. However, to the best of our knowledge, until now there is no research on how AMHP2012 is implemented and whether it affects protecting occupational health.

Heat-health warning systems

Heat-health warning systems (HHWSs) were developed to cope with impending hazardous hot weather and to provide advice on protecting health from extreme heat evens [69]. The HHWSs have been widely deployed in many areas around the world [70, 71]. The operation of an HHWS involves local weather forecasting and extreme weather identification, the determination of specific and sensitive trigger threshold, risk communication and actions recommendation [60, 72, 73].

Figure 7 shows the typical process within an HHWS. The standard for triggering warnings varies based upon differential nature of heat-health relationships in different local scales. Defining accurate locally-specific temperature thresholds is particularly significant for issuing heat warnings, as well as timely risk communication and public health interventions [69]. In many settings, the prediction of health consequence due to heat waves is feasible based on developed associations between extreme heat events and adverse health outcomes [74]. An effective HHWS would inform the public on how to achieve health protection and stay safe during extremely hot days.

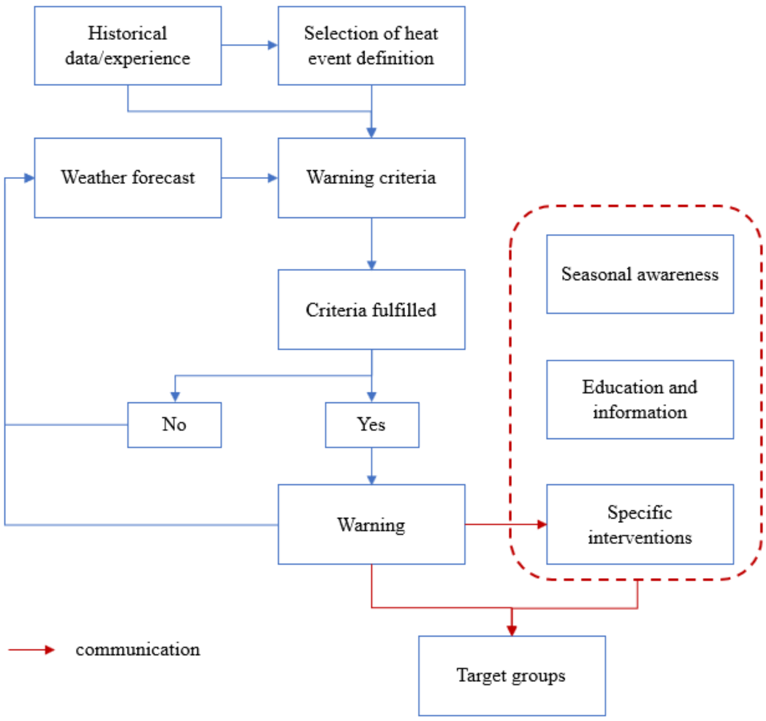


Figure 7. Flow diagram is displaying the operation of a typical heat-health warning system. Adapted from: [75].

In China, HHWSs have been set up in several cities such as Shanghai, Nanjing and Harbin. According to the stipulations of the National Emergency Response Plan for Public Health Emergencies released by the State Council of China in 2006, China has a four-tier warning including extremely serious, serious, major and ordinary levels. Red alert represents the most severe, followed by the orange, yellow and blue alert. In

Shanghai, HHWS was established in 2001 and are triggered when air-mass with higher mortality level is predicted [76]. A series of operations, such as risk dissemination through various media, health education, mobilization of medical and public services, maintenance of water and cooling facilities, are performed by the Shanghai Municipal Health Bureau, collaboration with other supporting agencies. Compared with 1998 heat wave, it is suggested that the successful implementation of HHWS in Shanghai was responsible for lower mortality in the 2003 heat wave [64].

Risk communication and behaviour change

It is difficult for the institutional arrangement to achieve an effective response to heat events without individual participation. The public should know what heat waves are, which health effects of heat waves they may be sensitive to, and what actions they can take to protect themselves from heat events [60]. However, a unique challenge in risk communication about heat waves exists in a public health campaign due to the following reasons [31]. First, unlike other disasters, heat waves are less sudden and dramatic. Second, the hazards posed by heat waves gradually aggravate as the exposure duration extends, because the ability of a person to tolerate excessive high temperature will gradually diminish. Moreover, one has perceived threats to heat waves also gradually diminishes with the duration of heat waves, and this will lead to demotivation of adaptive behaviours.

Fundamentally, whether risk communication and other interventions lead to changes in individual behaviour are the key to determining whether public health can successfully prevent heat-related mortality and morbidity [31]. Although extremely high temperatures could be lethal, the public is not well aware of the dangers of heat exposure. Many people at risk do not know their dangerous situation or are reluctant to take countermeasures [77]. Some people might know heat risks, but their knowledge of adaptative behaviour is limited [78]. Additionally, economic factors can hinder adaptative behaviours. For those who live on a fixed income or with low social, economic status, air-conditioning cooling during high temperatures means a big economic burden, and many of them would rather tolerate with heat waves than pay for air-conditioning. Worse still, some of them do not even have any cooling facilities in their home [79].

Therefore, a sound and concrete risk communication and public education program are necessary, especially in transforming risk perception into behavioural adaptation. Public health activities should raise not only general awareness of heat waves but also offer practical advice and indeed help [60]. The World Health Organization recommends that risk communication should actively reach out to vulnerable groups, constantly pay attention to their health status, and provide them with advice on heatstroke prevention and cooling, instead of just distributing brochures [73].

Provision of healthcare and social services

A heat warning system alone will not save lives without effective interventions and services that are prompted by the warning. The delivery of healthcare services is challenged in summer especially during extreme heat events, when it is necessary to achieve maximum coverage of the population, reaching the poor and socially vulnerable [60]. Working in hot environments can potentially threaten the health of workforces as well. Health workers may be reluctant to work when a severe heat wave comes, although the situations will harm their health and safety. Such reluctance will further exert pressure on the health care system, which is already overcrowded and stretched [80]. Therefore, hospitals, emergency centres, and public health system should consider hiring more health workers and increase their work shifts during hot days.

Social isolation and other adverse social factors can further deteriorate vulnerability to heat [81, 82], and the health sector should consider them. Healthcare delivery should match to the demands of the most vulnerable populations by the collaboration among health sectors, social departments, and other community-based organizations. The most appropriate plan is to recognize the most advisable and suitable choices by the structure of local healthcare and social service systems [60, 73]. Bell [83] suggested a whole-of systems approach for climate change including five areas or domains of health services: governance and culture, service delivery, workforce development, material infrastructure and finance (Figure 8). This approach may provide a useful framework in terms of involving a wide range of health and community services that could feasibly be part of government or community responses to heat waves.

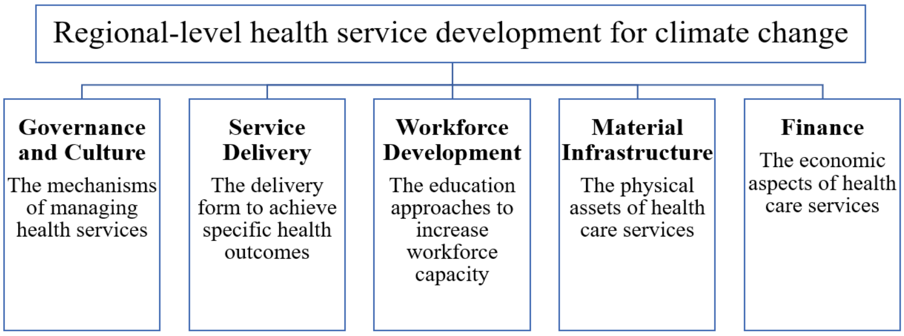


Figure 8. Definition of a whole-of-systems approach to developing health services for climate change. Adapted from: [83].

Heat exposure reduction

Reducing personal heat exposure is an important protection measure during extremely hot days. Due to the limitation of physiological adaption capacities, there is a limit to the extent of heat exposure that one can bear with [73, 81, 84]. Staying in a cool place can strongly protect the population from heat-related illnesses and deaths

[31]. Strategies include access to natural ventilation, air conditioning and cooling centres.

Natural ventilation, including using fans or opening window, is a long-standing strategy to reduce heat exposure. However, Ravanelli et al. [85] suggested that working fans are less effective and even harmful when the ambient temperature or relative humidity (RH) excessing a certain limit (e.g., upper limits were 80% relative humidity at 37 °C or 50% relative humidity at 42 °C in the USA). This might because without air-conditioning, fans were circulating hot air rather than cool air. Beyond the threshold, fans may increase heat stress by evaporating sweat and blowing hot air over the skin.

Air-conditioning has been proved to reduce heat-related mortality effectively. Previous studies revealed that heat-mortality decreased with household air-conditioning widespread in Chinese cities [64, 86]. However, some researchers oppose the frequent use of air-conditioning. For one reason, air conditioners emit waste heat to an outdoor environment during operation. Ohashi et al. [87] estimated the waste heat is causing a higher temperature in Tokyo office areas by 1-2 ℃ or more on weekdays. For the other reason, relying on air-conditioners may increase population vulnerability. Once blackout occurs and air-conditioning is not available, individuals who have come to depend on it may have trouble getting through heat waves by other means. Lin et al. [88] found a stronger adverse effect of the blackout in New York City in 2003 than on comparable hot days.

Access to cooling centres is another efficient way to reduce heat exposure [45]. In China, cooling centres have been set up by the Office of Civil Air Defense since the 21st century. A total of 153 cooling centres built in Henan Province can accommodate 210,000 people at a time. Centres will open from July to September during the daytime, or available to the public when the daily temperature exceeds the maximum daytime temperature of 35 ℃ or the minimum nighttime temperature of 28 ℃. Centres are equipped with air conditioning, drinking water, first aid medicines, recreational facilities, and even Wi-Fi in certain centres. However, there are barriers to access cooling centres, including concerns about pet care issues, inconvenient or unaffordable transportation, and loneliness of leaving home [25]. Among these concerns, transportation is raised as both resource and barrier to cooler places. An underlying concern is that public transportation may fail to send people to centres directly, waiting at the bus stop outside can even increase heat exposure, thus acting as a barrier to reaching cooling sites.

Urban planning for the cool city

The urban heat island is a phenomenon that urban regions experience warmer temperatures than surrounding areas due to the rapid urbanization. However, appropriate planning, such as "cool city" initiatives, could assist in reducing vulnerability, establishing resilience and promoting health [89]. The cool cities initiatives are drawing more attention for their potentialities to decrease morbidity and mortality of heat-related diseases, lower energy consumption, greenhouse gas emissions, air-conditioner use, and potentially enhance population health status. Strategies include optimizing building design, building parks and green spaces.

Optimizing building construction is one of the main strategies to achieve cool cities initiatives. Strategies for better building construction include two categories: increasing evapotranspiration and albedo. Increasing evapotranspiration is accomplished through green roofs to cool inside by the evaporation of water from vegetations. Increasing albedo is usually achieved by high reflectivity and light-coloured materials on roofs, which can increase building reflectivity, acting as a barrier to outside heat [60].

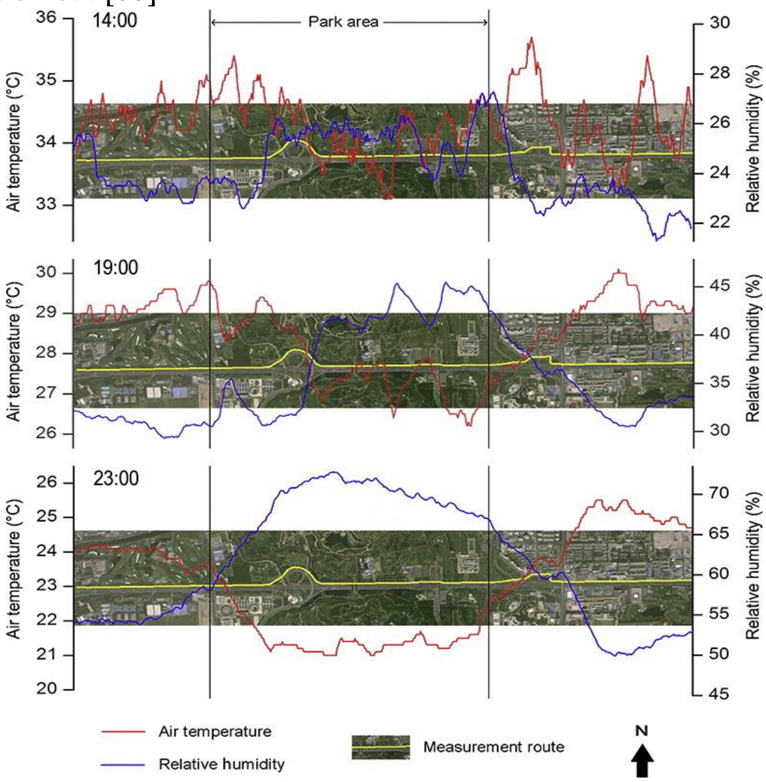


Figure 9. The distribution pattern of temperature and humidity inside and outside the park in Beijing, China. Source: [90].

Tree planting is commonly used to build shaded space in urban areas. Seeking shade is one of the main adaptive behaviours that people take when they are outdoor [91, 92]. Trees have multiple roles, for example blocking solar radiation, purifying the air, providing venues of outdoor sports, social and cultural activities [93, 94]. Yan et al. [90] demonstrated the significant cooling effects of a large urban park, and the cooling effects could expand to surrounding areas (Figure 9). Besides improving thermal comfort, providing access to green spaces can help promote public physical activity and social communications [95, 96]. Moderate intensity physical activities have been demonstrated to decrease all-cause mortality, morbidity of chronic non-communicable diseases such as cardio-cerebral vascular disease, diabetes, overweight and obesity, as well as mortality and morbidity of cancer [97, 98].

Vulnerability mapping

Vulnerability to heat is conceptualized to reflect population heat exposure and sensitivity. Vulnerability mapping is an emerging research field to characterize the population vulnerability, aiming at preventing heat-related health effects among vulnerable groups. Since not all populations have the same health risk from heat exposure, it is necessary to highlight areas with elevated vulnerability and identify the location of vulnerable people. Specific interventions can then be designed, which can help the government target their resources more efficiently and effectively. Recognizing community-level heat vulnerability not only gathers evidence from epidemiological studies on individual level susceptibility factors, but it also provides information about neighbourhood characteristics, thereby enabling more informed preventive actions. A national map of district-level heat vulnerability allows the government to situate vulnerable people to heat exposure and identify areas most in need of intervention.

Wolf et al. [99] suggested four steps to develop a vulnerability map. First, vulnerability values are calculated through a variance weighted approach. Second, values are mapped at a fine spatial scale. Third, to classify and identify the spatial cluster regions where vulnerability may occur. Last, it is necessary to assess the degree to which areas of high heat vulnerability coincide with possible areas of high heat exposure. In China, one previous study reported the spatial heterogeneity of social vulnerability to heat waves among 124 counties/districts of Guangdong Province [100]. Even a small-scale district shows a great variation invulnerability, which is inconsistent with the general distribution of vulnerability index in the whole Province. This inconsistency would be due to the differences in economic development levels in different districts, where well-developed economy region shows low social vulnerability to heat waves (Figure 10). This finding indicates the importance and necessity of taking city-specific social and economic characteristics into consideration for vulnerability evaluation.

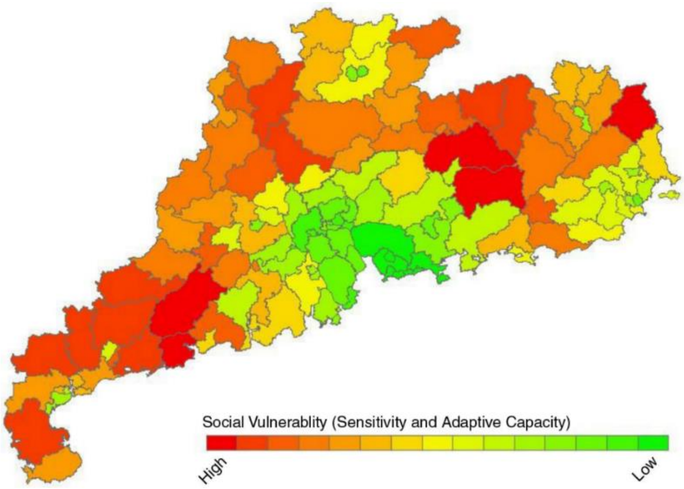


Figure 10. Social vulnerability to heat waves in Guangdong Province, China. Source: [100].

Surveillance, monitoring and evaluation

Real-time surveillance systems can be used to detect heat-related health threats in the early stage and inform health policy-makers about upcoming outbreaks of adverse health impacts due to the heat waves. The most useful real-time data are mortality data, ambulance calls, emergency department visits and general practitioner records. Among these, mortality data can provide detailed information about the impacts of heat events, acting as an important source. The lesson learned from the heat wave in Europe during 2003 indicated that timely feedback is essential for health sectors. Emergency department data may provide information about the non-fatal diseases that are susceptibility to the heat. Ambulance calls can provide the most timely information because of their sensibility to extreme heat [73, 101]. There is also a demand to design efficient syndromic surveillance systems for promoting public health responses to heat events [102]. Syndromic surveillance is the procedure of near real-time collection, analysis, interpretation and communication of health-related data. However, health data for surveillance need to readily available because the mortality and morbidity may increase rapidly after heat exposure [102]. These indicators could be taken into account as a public health "sentinel" indicator for triggering suitable interventions and eventually preventing adverse outcomes [38]. Long-term records of syndromic surveillance data can contribute to the developing and improving interventions focused on vulnerable populations.

Monitoring and evaluation can promote identification of the most effective interventions, both in the country- or local-scale, and barriers to implementation. For the adjustment of existing adaptation strategies, the iterative process can be followed based on continuous monitoring and evaluation (Figure 11). Epidemiology is a key approach to build the knowledge base for developing, implementing, and evaluating the effectiveness of public health adaptation to heat. However, evaluation of existing policies or measures is difficult because of the following reasons. Firstly, it may due to the regional disparity and time variation. Secondly, it is impossible to design a perfect study that considering all potential confounders. Randomized trials are usually infeasible for ethical and organizational reasons. In the meanwhile, observational studies have vital limitations because it is difficult to identify an appropriate control population and assess the appropriate type of intervention. Nevertheless, from both epidemiological and public health viewpoints, it is necessary to describe the changes occurring in the heat-health relationship over time. This information would assist policymakers in making evidence-based choices, in order to better allocate available resources and direct future research questions.

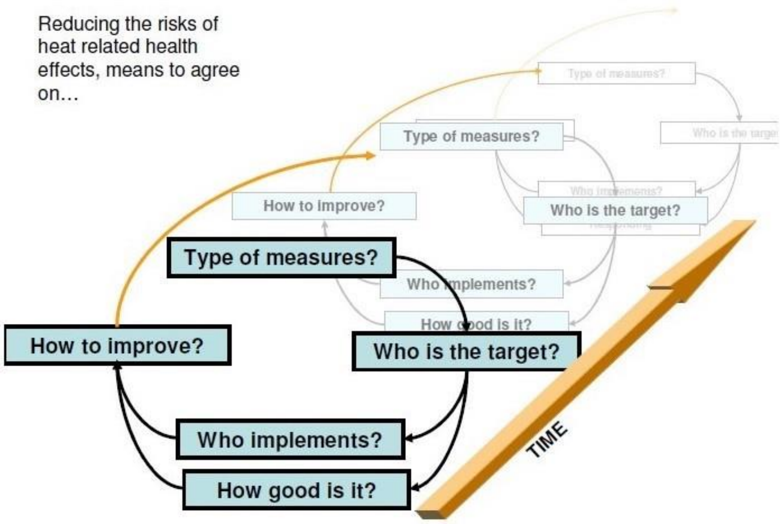


Figure 11. The iterative process for the development and assessment of public health adaptation strategies. Source: [73].

Conclusions

With more severe heat waves projected in the near future, evidence-based health protection measures by the general public and health professionals will play an important role in reducing heat-related disease burden. Planned adaptation strategies are becoming an increasing necessity for countries in the Asia-Pacific region to address the adverse health effects of extreme heat events. Heat vulnerability and adaptation assessments can highlight the significant gaps in understanding and managing the health impacts of heat waves in a changing climate.

References

1. Horton, R. M.; Mankin, J. S.; Lesk, C.; Coffel, E.; Raymond, C., A Review of Recent Advances in Research on Extreme Heat Events. Current Climate Change Reports 2016, 2, (4), 242-259.
2. Yiling He, C. H., Overlooked morbidity indicator: consequence from increasing ambulance dispatches associated with high ambient temperatures. Under submission 2019.
3. Bao, J.; Guo, Y.; Wang, Q.; He, Y.; Ma, R.; Hua, J.; Jiang, C.; Morabito, M.; Lei, L., et al., Effects of heat on first-ever strokes and the effect modification of atmospheric pressure: A time-series study in Shenzhen, China. Sci Total Environ 2019, 654, 1372-1378.
4. Qiong Wang, Q. L., Changchang Li, Meng Ren, Shao Lin, Luke D. Knibbs, Huanhuan Zhang, Wei Gong, Junzhe Bao, Suhan Wang, Xuemei Wang, Qingguo Zhao, Cunrui Huang, Interaction of Air Pollutants and Meteorological Factors on Birth Weight in Shenzhen, China. Epidemiology 2019. (In press)
5. Liu, T.; Ren, Z.; Zhang, Y.; Feng, B.; Lin, H.; Xiao, J.; Zeng, W.; Li, X.; Li, Z., et al., Modification Effects of Population Expansion, Ageing, and Adaptation on Heat-Related Mortality Risks Under Different Climate Change Scenarios in Guangzhou, China. Int J Environ Res Public Health 2019, 16, (3).
6. Dang, T. N.; Honda, Y.; Van Do, D.; Pham, A. L. T.; Chu, C.; Huang, C.; Phung, D., Effects of Extreme Temperatures on Mortality and Hospitalization in Ho Chi Minh City, Vietnam. Int J Environ Res Public Health 2019, 16, (3).
7. Phung, D.; Chu, C.; Tran, D. N.; Huang, C., Spatial variation of heat-related morbidity: A hierarchical Bayesian analysis in multiple districts of the Mekong Delta Region. Sci Total Environ 2018, 637-638, 1559-1565.
8. Huang, C.; Cheng, J.; Phung, D.; Tawatsupa, B.; Hu, W.; Xu, Z., Mortality burden attributable to heatwaves in Thailand: A systematic assessment incorporating evidence-based lag structure. Environ Int 2018, 121, (Pt 1), 41-50.
9. Sheng, R.; Li, C.; Wang, Q.; Yang, L.; Bao, J.; Wang, K.; Ma, R.; Gao, C.; Lin, S., et al., Does hot weather affect work-related injury? A case-crossover study in Guangzhou, China. Int J Hyg Environ Health 2018, 221, (3), 423-428.
10. Ma, R.; Zhong, S.; Morabito, M.; Hajat, S.; Xu, Z.; He, Y.; Bao, J.; Sheng, R.; Li, C., et al., Estimation of work-related injury and economic burden attributable to heat stress in Guangzhou, China. Science of The Total Environment 2019, 666, 147-154.
11. Maggie Bailey; Chrissy Esposito; Brian Clark; Foster, C.; Goeken, D.; Hanel, J.; Johnson, E.; Schmitt, S. Colorado's Climate and Colorado's Health Examining the Connection; Courtesy of the Colorado Health Institute: July 10, 2017, 2017.
12. Ye, X.; Wolff, R.; Yu, W.; Vaneckova, P.; Pan, X.; Tong, S., Ambient temperature and morbidity: a review of epidemiological evidence. Environ Health Perspect 2012, 120, (1), 19-28.
13. Gu, S.; Huang, C.; Bai, L.; Chu, C.; Liu, Q., Heat-related illness in China, summer of 2013. Int J Biometeorol 2016, 60, (1), 131-7.
14. Kan, H., Climate change and human health in China. Environ Health Perspect 2011, 119, (2), A60-1.
15. Petkova, E. P.; Morita, H.; Kinney, P. L., Health impacts of heat in a changing climate: how can emerging science inform urban adaptation planning? Curr Epidemiol Rep 2014, 1, (2), 67-74.
16. Gronlund, C. J., Racial and socioeconomic disparities in heat-related health effects and their mechanisms: a review. Curr Epidemiol Rep 2014, 1, (3), 165-173.

17. Kjellstrom, T.; Briggs, D.; Freyberg, C.; Lemke, B.; Otto, M.; Hyatt, O., Heat, Human Performance, and Occupational Health: A Key Issue for the Assessment of Global Climate Change Impacts. Annu Rev Public Health 2016, 37, 97-112.
18. 1Charbotel, B.; Fervers, B.; Droz, J. P., Occupational exposures in rare cancers: A critical review of the literature. Crit Rev Oncol Hematol 2014, 90, (2), 99-134.
19. Gubernot, D. M.; Anderson, G. B.; Hunting, K. L., Characterizing occupational heat-related mortality in the United States, 2000-2010: an analysis using the Census of Fatal Occupational Injuries database. Am J Ind Med 2015, 58, (2), 203-11.
20. Beck, N.; Balanay, J. A. G.; Johnson, T., Assessment of occupational exposure to heat stress and solar ultraviolet radiation among groundskeepers in an eastern North Carolina university setting. J Occup Environ Hyg 2018, 15, (2), 105-116.
21. Bartlett, S.; Larrieu, S.; Carcaillon, L.; Lefranc, A.; Helmer, C.; Dartigues, J.; Tavernier, B.; Ledrans, M.; Filleul, L., et al., Climate change and urban children: impacts and implications for adaptation in low- and middle-income countries Factors associated with morbidity during the 2003 heat wave in two population-based cohorts of elderly subjects: PAQUID and Three City Occupational heat illness in Washington State, 1995-2005. Environment and Urbanization 2008, 20, (2), 501-519.
22. Knowlton, K.; Rotkin-Ellman, M.; King, G.; Margolis, H. G.; Smith, D.; Solomon, G.; Trent, R.; English, P., The 2006 California heat wave: impacts on hospitalizations and emergency department visits. Environ Health Perspect 2009, 117, (1), 61-7.
23. Lee, S.; Lee, H.; Myung, W.; Kim, E. J.; Kim, H., Mental disease-related emergency admissions attributable to hot temperatures. Sci Total Environ 2018, 616-617, 688-694.
24. Thomas, C. L., - Fatal Isolation: The Devastating Paris Heat Wave of 2003, by Richard C. Keller. Psychiatry 2016, 79, (2), 180-183.
25. Sampson, N. R.; Gronlund, C. J.; Buxton, M. A.; Catalano, L.; White-Newsome, J. L.; Conlon, K. C.; O'Neill, M. S.; McCormick, S.; Parker, E. A., Staying cool in a changing climate: Reaching vulnerable populations during heat events. Glob Environ Change 2013, 23, (2), 475-484.
26. Crandall, C. G.; Gonzalez-Alonso, J., Cardiovascular function in the heat-stressed human. Acta Physiol (Oxf) 2010, 199, (4), 407-23.
27. Hopp, S.; Dominici, F.; Bobb, J. F., Medical diagnoses of heat wave-related hospital admissions in older adults. Prev Med 2018, 110, 81-85.
28. Wang, Q.; Li, C.; Guo, Y.; Barnett, A. G.; Tong, S.; Phung, D.; Chu, C.; Dear, K.; Wang, X., et al., Environmental ambient temperature and blood pressure in adults: A systematic review and meta-analysis. Sci Total Environ 2017, 575, 276-286.
29. Arbuthnott, K. G.; Hajat, S., The health effects of hotter summers and heat waves in the population of the United Kingdom: a review of the evidence. Environ Health 2017, 16, (Suppl 1), 119.
30. Stollberger, C.; Lutz, W.; Finsterer, J., Heat-related side-effects of neurological and non-neurological medication may increase heatwave fatalities. Eur J Neurol 2009, 16, (7), 879-82.
31. Luber, G.; McGeehin, M., Climate change and extreme heat events. Am J Prev Med 2008, 35, (5), 429-35.
32. Sommet, A.; Durrieu, G.; Lapeyre-Mestre, M.; Montastruc, J. L.; Ctr, A. F. P., A comparative study of adverse drug reactions during two heat waves that occurred in France in 2003 and 2006. Pharmacoepidemiology and Drug Safety 2012, 21, (3), 285-288.
33. Zhao, L.; Lee, X.; Smith, R. B.; Oleson, K., Strong contributions of local background climate to urban heat islands. Nature 2014, 511, (7508), 216-9.
34. Madrigano, J.; Ito, K.; Johnson, S.; Kinney, P. L.; Matte, T.; Parsons, K., A Case-Only Study of Vulnerability to Heat Wave-Related Mortality in New York City (2000-2011) Human Thermal

Environments: The Effects of Hot, Moderate, and Cold Environments on Human Health, Comfort, and Performance. Environ Health Perspect 2015, 123, (7), 672-8.
35. Sheng, R.; Li, C.; Wang, Q.; Yang, L.; Bao, J.; Wang, K.; Ma, R.; Gao, C.; Lin, S., et al., Does hot weather affect work-related injury? A case-crossover study in Guangzhou, China Comparing the Random Forest with the Generalized Additive Model to Evaluate the Impacts of Outdoor Ambient Environmental Factors on Scaffolding Construction Productivity. Int J Hyg Environ Health 2018, 221, (3), 423-428.
36. Laaidi, K.; Zeghnoun, A.; Dousset, B.; Bretin, P.; Vandentorren, S.; Giraudet, E.; Beaudeau, P., The impact of heat islands on mortality in Paris during the August 2003 heat wave. Environ Health Perspect 2012, 120, (2), 254-9.
37. Zhou, L.; Dickinson, R. E.; Tian, Y.; Fang, J.; Li, Q.; Kaufmann, R. K.; Tucker, C. J.; Myneni, R. B., Evidence for a significant urbanization effect on climate in China. Proc Natl Acad Sci U S A 2004, 101, (26), 9540-4.
38. Kravchenko, J.; Abernethy, A. P.; Fawzy, M.; Lyerly, H. K., Minimization of heatwave morbidity and mortality. Am J Prev Med 2013, 44, (3), 274-82.
39. Curriero, F. C.; Heiner, K. S.; Samet, J. M.; Zeger, S. L.; Strug, L.; Patz, J. A., Temperature and Mortality in 11 Cities of the Eastern United States. American Journal of Epidemiology 2002, 155, (1), 80-87.
40. Chan, E. Y. Y.; Goggins, W. B.; Kim, J. J.; Griffiths, S. M., A study of intracity variation of temperature-related mortality and socioeconomic status among the Chinese population in Hong Kong. Journal of epidemiology and community health 2012, 66, (4), 322-327.
41. Zhang, Y.; Nitschke, M.; Krackowizer, A.; Dear, K.; Pisaniello, D.; Weinstein, P.; Tucker, G.; Shakib, S.; Bi, P., Risk factors of direct heat-related hospital admissions during the 2009 heatwave in Adelaide, Australia: a matched case–control study. BMJ Open 2016, 6, (6).
42. Xu, Y.; Dadvand, P.; Barrera-Gomez, J.; Sartini, C.; Mari-Dell'Olmo, M.; Borrell, C.; Medina-Ramon, M.; Sunyer, J.; Basagana, X., Differences on the effect of heat waves on mortality by sociodemographic and urban landscape characteristics. Journal of epidemiology and community health 2013, 67, (6), 519-25.
43. Larrieu, S.; Carcaillon, L.; Lefranc, A.; Helmer, C.; Dartigues, J. F.; Tavernier, B.; Ledrans, M.; Filleul, L., Factors associated with morbidity during the 2003 heat wave in two population-based cohorts of elderly subjects: PAQUID and Three City. Eur J Epidemiol 2008, 23, (4), 295-302.
44. Zanobetti, A.; O'Neill, M. S.; Gronlund, C. J.; Schwartz, J. D., Susceptibility to mortality in weather extremes: effect modification by personal and small-area characteristics. Epidemiology 2013, 24, (6), 809-19.
45. Bouchama, A.; Dehbi, M.; Mohamed, G.; Matthies, F.; Shoukri, M.; Menne, B., Prognostic factors in heat wave related deaths: a meta-analysis. Arch Intern Med 2007, 167, (20), 2170-6.
46. Dosio, A.; Mentaschi, L.; Fischer, E. M.; Wyser, K., Extreme heat waves under 1.5 °C and 2 °C global warming. Environmental Research Letters 2018, 13, (5), 054006.
47. Chotamonsak, C.; Salathé Jr, E. P.; Kreasuwan, J.; Chantara, S.; Siriwitayakorn, K., Projected climate change over Southeast Asia simulated using a WRF regional climate model. Atmospheric Science Letters 2011, 12, (2), 213-219.
48. United Nations, D. o. E. a. S. A., Population Division (2018) World Urbanization Prospects: The 2018 Revision; 2018.
49. Heaviside, C.; Vardoulakis, S.; Cai, X. M., Attribution of mortality to the urban heat island during heatwaves in the West Midlands, UK. Environ Health 2016, 15 Suppl 1, 27.
50. Yang, J.; Siri, J. G.; Remais, J. V.; Cheng, Q.; Zhang, H.; Chan, K. K. Y.; Sun, Z.; Zhao, Y.; Cong, N., et al., The Tsinghua– Lancet Commission on Healthy Cities in China: unlocking the power of cities for a healthy China. The Lancet 2018, 391, (10135), 2140-2184.

51. United Nations, E. a. S. C. f. A. a. t. P. ESCAP Population Data Sheet 2018; 2018.
52. United Nations, D. o. E. a. S. A., Population Division World Population Prospects: The 2017 Revision, Online Demographic Profiles; 2017.
53. Gasparrini, A.; Guo, Y.; Hashizume, M.; Lavigne, E.; Zanobetti, A.; Schwartz, J.; Tobias, A.; Tong, S.; Rocklov, J., et al., Mortality risk attributable to high and low ambient temperature: a multicountry observational study. Lancet 2015, 386, (9991), 369-75.
54. Sherwood, S. C.; Huber, M., An adaptability limit to climate change due to heat stress. Proc Natl Acad Sci U S A 2010, 107, (21), 9552-5.
55. Hawks, J.; Wang, E. T.; Cochran, G. M.; Harpending, H. C.; Moyzis, R. K., Recent acceleration of human adaptive evolution. Proc Natl Acad Sci U S A 2007, 104, (52), 20753-8.
56. Kjellstrom, T.; Holmer, I.; Lemke, B., Workplace heat stress, health and productivity - an increasing challenge for low and middle-income countries during climate change. Glob Health Action 2009, 2, 46-51.
57. Zander, K. K.; Botzen, W. J. W.; Oppermann, E.; Kjellstrom, T.; Garnett, S. T., Heat stress causes substantial labour productivity loss in Australia. Nat Clim Change 2015, 5, (7), 647.
58. McMichael, A. J.; Dear, K. B., Climate change: heat, health, and longer horizons. Proc Natl Acad Sci U S A 2010, 107, (21), 9483-4.
59. Huang, C.; Vaneckova, P.; Wang, X.; Fitzgerald, G.; Guo, Y.; Tong, S., Constraints and barriers to public health adaptation to climate change: a review of the literature. Am J Prev Med 2011, 40, (2), 183-90.
60. Huang, C.; Barnett, A. G.; Xu, Z.; Chu, C.; Wang, X.; Turner, L. R.; Tong, S., Managing the health effects of temperature in response to climate change: challenges ahead. Environ Health Perspect 2013, 121, (4), 415-9.
61. Bernard, S. M.; McGeehin, M. A., Municipal heat wave response plans. Am J Public Health 2004, 94, (9), 1520-2.
62. Matthies, F.; Menne, B., Prevention and management of health hazards related to heatwaves. Int J Circumpolar Health 2009, 68, (1), 8-22.
63. Chau, P. H.; Chan, K. C.; Woo, J., Hot weather warning might help to reduce elderly mortality in Hong Kong. Int J Biometeorol 2009, 53, (5), 461-8.
64. Tan, J.; Zheng, Y.; Song, G.; Kalkstein, L. S.; Kalkstein, A. J.; Tang, X., Heat wave impacts on mortality in Shanghai, 1998 and 2003. Int J Biometeorol 2007, 51, (3), 193-200.
65. Fouillet, A.; Rey, G.; Wagner, V.; Laaidi, K.; Empereur-Bissonnet, P.; Le Tertre, A.; Frayssinet, P.; Bessemoulin, P.; Laurent, F., et al., Has the impact of heat waves on mortality changed in France since the European heat wave of summer 2003? A study of the 2006 heat wave. International journal of epidemiology 2008, 37, (2), 309-17.
66. Price, K.; Perron, S.; King, N., Implementation of the Montreal heat response plan during the 2010 heat wave. Canadian Journal of public health = Revue Canadienne de Sante Publique 2013, 104, (2), e96-100.
67. Benmarhnia, T.; Bailey, Z.; Kaiser, D.; Auger, N.; King, N.; Kaufman, J. S., A Difference-in-Differences Approach to Assess the Effect of a Heat Action Plan on Heat-Related Mortality, and Differences in Effectiveness According to Sex, Age, and Socioeconomic Status (Montreal, Quebec). Environ Health Perspect 2016, 124, (11), 1694-1699.
68. Price, K.; Benmarhnia, T.; Gaudet, J.; Kaiser, D.; Sadoine, M. L.; Perron, S.; Smargiassi, A., The Montreal heat response plan: evaluation of its implementation towards healthcare professionals and vulnerable populations. Canadian Journal of public health = Revue Canadienne de Sante Publique 2018, 109, (1), 108-116.
69. Hajat, S.; Sheridan, S. C.; Allen, M. J.; Pascal, M.; Laaidi, K.; Yagouti, A.; Bickis, U.; Tobias, A.; Bourque, D., et al., Heat-health warning systems: a comparison of the predictive capacity of

different approaches to identifying dangerously hot days. Am J Public Health 2010, 100, (6), 1137-44.
70. O'Neill, M. S.; Ebi, K. L., Temperature extremes and health: impacts of climate variability and change in the United States. J Occup Environ Med 2009, 51, (1), 13-25.
71. Toloo, G. S.; Fitzgerald, G.; Aitken, P.; Verrall, K.; Tong, S., Are heat warning systems effective? Environ Health 2013, 12, 27.
72. Lowe, D.; Ebi, K. L.; Forsberg, B., Heatwave early warning systems and adaptation advice to reduce human health consequences of heatwaves. International journal of environmental research and public health 2011, 8, (12), 4623-48.
73. WHO Improving public health responses to extreme weather/heat-waves : EuroHEAT : technical summary; WHO Regional Office for Europe: Copenhagen, 2009.
74. Gosling, S. N.; Lowe, J. A.; McGregor, G. R.; Pelling, M.; Malamud, B. D., Associations between elevated atmospheric temperature and human mortality: a critical review of the literature. Climatic Change 2009, 92, (3-4), 299-341.
75. Kalkstein, L., Heat Health Warning Systems: Definition and Methodology. 2012; p 28-42.
76. Tan, J.; Kalkstein, L. S.; Huang, J.; Lin, S.; Yin, H.; Shao, D., An operational heat/health warning system in Shanghai. Int J Biometeorol 2004, 48, (3), 157-62.
77. Lane, K.; Wheeler, K.; Charles-Guzman, K.; Ahmed, M.; Blum, M.; Gregory, K.; Graber, N.; Clark, N.; Matte, T., Extreme heat awareness and protective behaviors in New York City. Journal of urban health : bulletin of the New York Academy of Medicine 2014, 91, (3), 403-14.
78. Sheridan, S. C., A survey of public perception and response to heat warnings across four North American cities: an evaluation of municipal effectiveness. Int J Biometeorol 2007, 52, (1), 3-15.
79. Stuart, K.; Mahmood, M. A.; Clark, L.; Pace, R., Health education and a co-ordinated response system to support vulnerable people during heat waves. Aust N Z J Public Health 2011, 35, (4), 394-5; discussion 395.
80. Smith, E.; Morgans, A.; Qureshi, C.; Archer, F.; Burkle, S., Paramedics' perceptions of risk and willingness to work during disasters. Australian Journal of Emergency Management 2009, 24, (2), 14-20.
81. Kovats, R. S.; Hajat, S., Heat stress and public health: a critical review. Annu Rev Public Health 2008, 29, 41-55.
82. Hajat, S.; Kosatky, T., Heat-related mortality: a review and exploration of heterogeneity. Journal of epidemiology and community health 2010, 64, (9), 753-60.
83. Bell, E., Readying health services for climate change: a policy framework for regional development. Am J Public Health 2011, 101, (5), 804-13.
84. Hajat, S.; O'Connor, M.; Kosatsky, T., Health effects of hot weather: from awareness of risk factors to effective health protection. Lancet 2010, 375, (9717), 856-863.
85. Ravanelli, N. M.; Hodder, S. G.; Havenith, G.; Jay, O., Heart rate and body temperature responses to extreme heat and humidity with and without electric fans. JAMA 2015, 313, (7), 724.
86. 86. Ma, W.; Chen, R.; Kan, H., Temperature-related mortality in 17 large Chinese cities: how heat and cold affect mortality in China. Environ Res 2014, 134, 127-33.
87. Ohashi, Y.; Genchi, Y.; Kondo, H.; Kikegawa, Y.; Yoshikado, H.; Hirano, Y., Influence of air-conditioning waste heat on air temperature in Tokyo during summer: Numerical experiments using an urban canopy model coupled with a building energy model. Journal of Applied Meteorology and Climatology 2007, 46, (1), 66-81.
88. Lin, S.; Fletcher, B. A.; Luo, M.; Chinery, R.; Hwang, S. A., Health impact in New York City during the Northeastern blackout of 2003. Public Health Rep 2011, 126, (3), 384-93.

89. Stone, B.; Hess, J. J.; Frumkin, H., Urban form and extreme heat events: are sprawling cities more vulnerable to climate change than compact cities? Environ Health Perspect 2010, 118, (10), 1425-8.
90. Yan, H.; Wu, F.; Dong, L., Influence of a large urban park on the local urban thermal environment. Sci Total Environ 2018, 622-623, 882-891.
91. Ahmed, K. S., Comfort in urban spaces: defining the boundaries of outdoor thermal comfort for the tropical urban environments. Energy and Buildings 2003, 35, (1), 103-110.
92. Lin, T. P., Thermal perception, adaptation and attendance in a public square in hot and humid regions. Building and Environment 2009, 44, (10), 2017-2026.
93. Boone-Heinonen, J.; Casanova, K.; Richardson, A. S.; Gordon-Larsen, P., Where can they play? Outdoor spaces and physical activity among adolescents in U.S. urbanized areas. Prev Med 2010, 51, (3-4), 295-8.
94. van den Berg, A. E.; Maas, J.; Verheij, R. A.; Groenewegen, P. P., Green space as a buffer between stressful life events and health. Soc Sci Med 2010, 70, (8), 1203-10.
95. Hunter, R. F.; Christian, H.; Veitch, J.; Astell-Burt, T.; Hipp, J. A.; Schipperijn, J., The impact of interventions to promote physical activity in urban green space: a systematic review and recommendations for future research. Soc Sci Med 2015, 124, 246-56.
96. Schipperijn, J.; Bentsen, P.; Troelsen, J.; Toftager, M.; Stigsdotter, U. K., Associations between physical activity and characteristics of urban green space. Urban Forestry & Urban Greening 2013, 12, (1), 109-116.
97. Woodcock, J.; Edwards, P.; Tonne, C.; Armstrong, B. G.; Ashiru, O.; Banister, D.; Beevers, S.; Chalabi, Z.; Chowdhury, Z., et al., Public health benefits of strategies to reduce greenhouse-gas emissions: urban land transport. Lancet 2009, 374, (9705), 1930-43.
98. Monninkhof, E. M.; Elias, S. G.; Vlems, F. A.; van der Tweel, I.; Schuit, A. J.; Voskuil, D. W.; van Leeuwen, F. E.; Tfpac, Physical activity and breast cancer: a systematic review. Epidemiology 2007, 18, (1), 137-57.
99. Wolf, T.; McGregor, G., The development of a heat wave vulnerability index for London, United Kingdom. Weather and Climate Extremes 2013, 1, 59-68.
100. Zhu, Q.; Liu, T.; Lin, H.; Xiao, J.; Luo, Y.; Zeng, W.; Zeng, S.; Wei, Y.; Chu, C., et al., The spatial distribution of health vulnerability to heat waves in Guangdong Province, China. Glob Health Action 2014, 7, 25051.
101. Turner, L. R.; Connell, D.; Tong, S., Exposure to hot and cold temperatures and ambulance attendances in Brisbane, Australia: a time-series study. BMJ Open 2012, 2, (4).
102. Leonardi, G. S.; Hajat, S.; Kovats, R. S.; Smith, G. E.; Cooper, D.; Gerard, E., Syndromic surveillance use to detect the early effects of heat-waves: an analysis of NHS direct data in England. Sozial- und Praventivmedizin 2006, 51, (4), 194-201.

Appendix

1. Agenda of *APN Workshop: Climate Change and Health in the Asia-Pacific Region in 2016*

2. Agenda of *International Forum on Climate Change and Health Response & APN Network and Collaboration in 2017*

3. Agenda of *2nd International Forum on Climate Change and Health Response & APN Network and Collaboration in 2018*

APN Workshop: Climate Change and Health in the Asia-Pacific Region

Date: 25–27 November, 2016
Venue: Conference Room 2, Institute of State Governance, Sun Yat-sen University

Thursday, November 24, 2016			
12:00-18:00	**Conference Registration** (Venue: Conference Room 2, Institute of State Governance, Sun Yat-sen University, Guangzhou)		
Friday, November 25, 2016			
Welcome & Opening			
Chair: Cunrui Huang			
Country Reports			
8:40-9:00	Qiyong Liu	Climate change impacts on human health and adaptation in China (973 programs)	China CDC
9:00-9:15	Vijendra Ingole	The associations between Weather/temperature and population health in India	India
9:15-9:30	Benjwwan Tawatsupa	The impact of heat stress on occupational health in Thailand	Thailand
9:30-9:45	Tran Ngoc Dang	Attributable deaths due to urban heat island effect in a megacity of Vietnam	Vietnam/Japan
9:45-10:00	M.Mamun Huda	The Impact of Temperature on Human Health in Bangladesh	Bangladesh
10:00-10:15	Q&A		
10:15-10:40	Morning Tea		
10:45-11:00	Wenjun Ma	Impacts of climate change and air pollution on human health in Guangdong	GDCDC, China
11:00-11:15	Radwan Talukder	Safety of drinking water in the context of climate change and population health in Bangladesh	

		Bangladesh
11:15-11:30	Do Manh Cuong	The Impacts of massive saltwater intrusion and drought in Vietnam
		Vietnam
11:30-11:45	Dung Phung	Temperature and health effects in Vietnam
		Australia/Vietnam
11:45-12:00	Q&A	
12:00-14:00	Lunch	
Research Reports		
14:00-14:30	Weiwei Lin Qiong Wang	Air Pollution and Health effects: biomarker studies in susceptible populations
		Sun Yat-sen University
14:30-14:45	Junzhe Bao	Construction and validation of the heat vulnerability index
		Sun Yat-sen University
14:45-15:00	Lianping Yang	Health professionals preparedness regarding climate change in primary care
		Sun Yat-sen University
15:00-15:15	Q&A	
15:15-15:45	Afternoon Tea	
Dissertation Proposal		
15:45-16:00	Changchang Li	Exposure to extreme ambient temperature during pregnancy and the risk of early delivery
		Sun Yat-sen University
16:00-16:15	Rongrong Sheng	The associations between heat exposure, work-related injury and labour capacity in construction workers in China
		Sun Yat-sen University
16:15-16:30	Kaiwen Wang	Health risk assessment of tornado in China
		Sun Yat-sen University
16:30-17:00	Q&A	

APN Project		
17:00-17:20	Cunrui Huang	Assessing the health effects of extreme temperatures and the development of adaptation strategies to climate change Sun Yat-sen University
17:20-18:00	Discussion of first-day outcomes	
18:00-20:00	Welcome Dinner	
Saturday, November 26, 2016		
Collaboration Discussion		
8:30-10:00	Qiong Wang, Cunrui Huang	Risk assessments 1: Interaction effects of air pollution and climatic factors on health Sun Yat-sen University
10:00-10:30	Morning Tea	
10:30-12:00	Qiong Wang, Cunrui Huang	Risk assessments 2: Quantify the total mortality burden attributable to non-optimum ambient temperature in China, Vietnam, Thailand and Bangladesh Sun Yat-sen University
12:00-14:00	Lunch	
14:00-15:30	Junzhe Bao, Cunrui Huang	Vulnerability assessments 1: Identify vulnerable population and areas in the context of heat stress and air pollution Sun Yat-sen University
15:30-16:00	Afternoon Tea	
16:00-17:30	Junzhe Bao, Cunrui Huang	Vulnerability assessments 2: Examine whether temperature-related health risks varied according to individual and community characteristics Sun Yat-sen University
17:30-18:00	Discussion of second-day outcome	
18:00-20:00	Dinner	
Sunday, November 27, 2016		
8:30-10:00	Lianping Yang, Cunrui Huang	Adaptation strategies: Address health threatens of climate change using a primary care approach Sun Yat-sen University

10:00-10:30	Morning Tea	
10:30-12:00	Lianping Yang, Cunrui Huang	Adaptation strategies: Formulate local adaptation strategies for dealing with temperature-related health effects and reduce vulnerability
		Sun Yat-sen University
12:00-12:30	Discussion of workshop outcomes	
12:30:14:00	Lunch	
14:00-18:00	Sites Visit	
18:00-20:00	Dinner	
Monday, November 28, 2016		
	Check Out	


APN Workshop: Climate Change and Health
in the Asia-Pacific Region


岭南印象园


APN Workshop: Climate Change and Health in the Asia-Pacific Region
Guangzhou, China November 2016

International Forum on Climate Change and Health Response
& APN Network and Collaboration

Date: 9-12 December, 2017
Venue: Yihe Hotel, Guangzhou, China

December 9 Saturday		
15:00-20:00	**Registration** (Venue: Yihe Hotel, Tongtai Road, Baiyun District, Guangzhou 510440, China)	
18:30-21:00	**Icebreaker & welcome**	
December 10 Sunday 8:00-12:30		
Welcome & Opening		
Chair: Professor Yuantao Hao Dean of School of Public Health, Sun Yat-sen University, China		
7:50-8:35	Zhibin Yao	Vice Chairman, The Guangdong Provincial Committee of the People's Political Consultative Conference; President, The Medical Association of Guangdong Province, China
	Liangyou Wu	Director, Division of Chronic Diseases Prevention and Control, National Health and Family Planning Commission of China
	Wenjie Dong	Professor, Sun Yat-sen University; Scientific Committee Member, Asia-Pacific Network for Global Change Research (APN)
	Minbin Yu	Deputy Secretary of Party Committee, Sun Yat-sen University, China
	Zhen He	Vice Chairman, Guangdong Provincial Association for Science and Technology, China
Keynotes		
Chair: Professor Cunrui Huang School of Public Health, Sun Yat-sen University, China		
8:35-9:00	Panmao Zhai	Changes in extreme weather and climate events and the implications for human health
		Professor, Chinese Academy of Meteorological Sciences *Co-Chair, IPCC Working Group Ⅰ*
9:00-9:25	Kristie L. Ebi	Climate Change and Health: Current Status and Future Directions
		Professor, Center for Health and the Global Environment, University of Washington, USA
9:25-9:50	Wenjie Dong	Reversibility of historical and future climate change with a complex earth system model
		Professor, Dean of School of Atmospheric Sciences, Sun Yat-sen University, China; Scientific Committee Member, Asia-Pacific Network for Global Change Research (APN)
9:50-10:15	Raghu Murtugudde	Exciting Times Health Predictions and Projections

		Professor, Earth System Science Interdisciplinary Center University of Maryland at College Park, USA
10:15-10:45	Coffee & Tea break; Group photo	
Keynotes		
Chair: Professor Shaoxian Chen School of Public Health, Sun Yat-sen University, China		
10:45-11:10	Virginia Murray	Disaster risk management and the Sendai Framework – what is the role for disaster reduction, climate change and health resilience? *Consultant, UN Global Disaster Risk Reduction; Professor, Public Health England, UK*
11:10-11:35	Xiaoming Shi	Health Adaptation to Climate Change in China *Professor, Director of National Institute of Environment Health, China CDC*
11:35-12:00	Xin-Zhong Liang	Improving regional climate change projections with reliable uncertainty estimates for impact assessment *Professor, Head of Earth System Model Research and Development Lab, University of Maryland at College Park, USA*
12:00-12:25	Haidong Kan	Health effects of climate pollutants in China *Professor, Deputy Dean of School of Public Health, Fudan University, China*
12:30-14:00	Lunch	
December 10 Sunday 14:00-18:00		
Session 1: Climate change, heat stress, health and productivity		
Chair: Prof Haidong Kan School of Public Health, Fudan University, China		
14:00-14:20	Shakoor Hajat	Epidemiology of temperature-related health and its role in formulating policies on climate change *A/Professor, Dept. of Social & Environmental Health Research, London School of Hygiene and Tropical Medicine, UK*
14:20-14:40	Jeremy J. Hess	Heat Early Warning Systems and Action Plans: Building Evidence Related to Effectiveness and Implementation *A/Professor, Center for Health and the Global Environment, University of Washington, USA*
14:40-15:00	Marco Morabito	HEAT-SHIELD tools for protection of health and productivity in workplaces: new approaches to short-term warnings and long-term planning *Researcher, Institute of Biometeorology, National Research Council, Italy*
15:00-15:20	Yasushi Honda	Climate change impact on health - from S-14 project

		Professor, Faculty of Health and Sport Sciences University of Tsukuba, Japan
15:20-15:40	Chuansi Gao	Translating climate service into personalized adaptation strategies to cope with thermal climate stress
		A/Professor, Dept. of Design Sciences Lund University, Sweden
15:40-16:00	Tran Ngoc Dang	Education needs and knowledge on health impacts of climate change among medical students: a multi-countries proposal
		Lecturer, University of Medicine and Pharmacy at Ho Chi Minh City, Vietnam
16:00-16:30	Coffee & Tea break	
Panel discussion		
Chair: Professor Peng Bi School of Public Health, University of Adelaide, Australia		
16:30-17:45	Keith Dear	Professor, University of Adelaide, Australia
	Franz W. Gatzweiler	Professor, Institute of Urban Environment, Chinese Academy of Sciences, China
	Biraj Karmacharya	Chief, Department of Community Programs Dhulikhel Hospital, Kathmandu University, Nepal
	Dung Phung	Deputy Director, CEPH Coordinator for Vietnam Program, Griffith University, Australia
	Jing Wu	Professor, Director of Division of Chronic Disease Prevention and Community Health, China CDC
	Yaodong Du	Director, Guangdong Institute of Meteorology, China
	Wenjun Ma	Professor, Dean of Guangdong Institute of Public Health, China
18:00-20:00	Dinner	
December 11 Monday 9:00-12:30		
Session 2: Climate change, air pollution, and vulnerable groups		
Chair: Professor Xinbiao Guo School of Public Health, Peking University, China		
8:30-8:50	Kim Ho	Effects of air pollution on mental health associated with climate change
		Professor, Dean of Graduate School of Public Health Seoul National University, Korean
8:50-9:10	Shao Lin	Extreme Weather, Natural Disaster, Vulnerability and Human Health in NY
		Professor, School of Public Health, University at Albany State University of New York, USA

9:10-9:30	Xuemei Wang	Impacts of Atmospheric Mercury/Lead Deposition on Human Multimedia Exposure: Projection from Observations in the Pearl River Delta Region, South China
		Professor, Vice Dean of Institute for Environmental and Climate Research, Jinan University, China
9:30-9:50	Amir Sapkota	Extreme weather events, Population Vulnerability, and Impaired Health: How Do We Move Forward?
		A/Professor, School of Public Health University of Maryland, College Park, USA
9:50-10:10	Luke Knibbs	The effects of climate and air pollution on people with chronic lung disease in Australia
		Senior Lecturer, School of Public Health University of Queensland, Australia
10:10-10:30	Linwei Tian	Relationship of air pollution with pneumonia mortality modified by urban climate
		A/Professor, School of Public Health The University of Hong Kong, Hong Kong, China
10:30-11:00	Coffee & Tea break	
Panel discussion		
Chair: Professor Shao Lin School of Public Health, State University of New York at Albany, USA		
11:00-12:15	Xinbiao Guo	Professor, Director of Dept. of Occupational and Environmental Health, School of Public Health, Peking University, China
	Shi Liang	Deputy Director, Shenzhen Prevention and Treatment Centre for Occupational Diseases, China
	Febi Dwirahmadi	Lecturer, CEPH Coordinator for Indonesian Program, Griffith University, Australia
	Victor Hoe	Professor, Department of Social and Preventive Medicine, Faculty of Medicine, University of Malaya, Malaysia
	Ta-Yuan Chang	Professor & Chairperson, Department of Occupational Safety and Health, China Medical University, Taiwan, China
	Xiangqian Lao	Professor, The Jockey Club School of Public Health and Primary Care, Chinese University of Hong Kong, China
	Mohammad Sohel Shomik	Coordinator, Centre for Communicable Diseases, International Centre for Diarrheal Disease Research, Bangladesh
12:30-14:00	Lunch	
December 11 Monday 14:00-18:00		
Session 3: Promoting awareness and strengthening health resilience to climate change		
Chair: Cordia Chu Centre for Environment and Population Health, Griffith University, Australia		
14:00-14:20	Tarik Benmarhnia	Using Natural Experiments to evaluate the Potential Health Benefits of Adaptation Policies Related to Extreme Weather Events

		Assistant Professor, Department of Family Medicine and Public Health & Scripps Institution of Oceanography, University of California, USA
14:20-14:40	Peng Bi	Addressing the public health impact of climate change-associated infectious diseases in China
		Professor, School of Public Health, University of Adelaide, Australia
14:40-15:00	Sam Sellers	Health Systems Under the Shared Socioeconomic Pathways
		Senior Fellow, Center for Health and the Global Environment, University of Washington, USA
15:00-15:20	Ronald P. Law	Putting Climate and Disaster Resilience into the Health Agenda: The Philippine Experience
		Chief, Preparedness Division, Health Emergency Management Bureau, Department of Health, Philippines
15:20-15:40	Wenbiao Hu	Towards developing an early warning system for infectious diseases
		A/Professor, School of Public Health and Social Work Queensland University of Technology, Australia
15:40-16:00	Ying Zhang	Perceptions of environmental and climate changes in remote mountain villages of ethnic minorities in Hubei Province, China
		Senior Lecturer, School of Public Health, University of Sydney, Australia
16:00-16:30	Coffee & Tea break	
Panel discussion		
Chair: Dr Ying Zhang School of Public Health, University of Sydney, Australia		
16:30-17:45	Cordia Chu	Director, Centre for Environment and Population Health Griffith University, Australia
	Nguyen Dinh Cuong	National Team Leader, Conseil Sante, Vietnam
	Arif Wibowo	Deputy Director, Climate Change Vulnerability Assessment Ministry of Environment and Forestry, Indonesia
	Wei Ma	Professor, School of Public Health, Shandong University, China
	Xiangzheng Lv	Managing Editor, *Chinese Journal of Preventive Medicine*
	Daoxin Yin	Editor, *The BMJ (British Medical Journal)*
	James Zhang	Managing Editor, *Int J Environ Res Public Health*
	Tianshu Li	Chief Reporter, *Health News*, China
18:00-20:00	Dinner	
20:00-21:00	Pearl River Night Cruise	

December 12 Tuesday (by invitation only)	
08:30-10:30	**APN network and collaboration**
10:30-10:50	Coffee & Tea break
10:50-12:00	**Round table discussion**
12:00-12:20	**Closing ceremony**
12:20-13:30	Lunch
13:30-18:00	**Guangzhou City Tour**
18:00-20:00	Dinner


GUANGZHOU
“一带一路”气候变化与健康应对高峰论坛


GUANGZHOU
CHINA 2017
“一带一路”气候变化
SUMMIT FORUM ON CLIMATE CHANGE AND HEALTH R
广东省科学技术协会
JANGDONG PROVINCIAL ASSOCIATION FO
KER：SCHOOL OF PUBLIC HEALTH, SUN Y
SOR：


黄存瑞
翟盘茂
Kristie L. Ebi
Raghu Murtugudde

2nd International Forum on Climate Change and Health Response & APN Network and Collaboration

Date: 2-4 December, 2018
Venue: The Asia International Hotel, Guangzhou, China

<table>
<tr><td colspan="3">Saturday, 1st December 2018</td></tr>
<tr><td>15:00-20:00</td><td colspan="2">Registration
Lobby of The Asia International Hotel
No. 326 Huanshi East Road, Yuexiu District, Guangzhou, China</td></tr>
<tr><td colspan="3">Sunday Morning, 2nd December 2018</td></tr>
<tr><td>8:00-8:15</td><td colspan="2">On-Site Registration
Conference Venue: Asia Palace, 8th Floor, The Asia International Hotel</td></tr>
<tr><td colspan="3">Welcome & Opening</td></tr>
<tr><td colspan="3">Chair: Wenjie DONG
Professor and Dean of School of Atmospheric Sciences, Sun Yat-sen University, China</td></tr>
<tr><td rowspan="3">8:15-8:40</td><td colspan="2">Representative of Sun Yat-sen University, China</td></tr>
<tr><td>Shanchao Wu</td><td>Deputy Director of Department of Research and Publicity,
China Association for Science and Technology, China</td></tr>
<tr><td>Wenjie Dong</td><td>Dean of School of Atmospheric Sciences, Sun Yat-sen University, China;
Scientific Committee Member, Asia-Pacific Network for Global Change Research (APN)</td></tr>
<tr><td>8:40-8:45</td><td colspan="2">Review of the 1st International Forum</td></tr>
<tr><td>8:45-9:00</td><td colspan="2">Group Photo</td></tr>
<tr><td colspan="3">Sunday Morning, 2nd December 2018</td></tr>
<tr><td colspan="3">KEYNOTES: Advances in Climate Change and Health Research</td></tr>
<tr><td colspan="3">Chair: Cunrui HUANG
Professor, School of Public Health, Sun Yat-sen University, China</td></tr>
<tr><td rowspan="2">9:00-9:25</td><td rowspan="2">Peng Gong</td><td>Some Research Questions on Healthy Cities Development</td></tr>
<tr><td>Professor and Department Chair of Earth System Science,
Tsinghua University, China</td></tr>
<tr><td>9:25-09:50</td><td>Raghu Murtugudde</td><td>Monsoon Extremes and Human Health</td></tr>
</table>

		Professor, Atmospheric and Oceanic Science and Earth System Science, University of Maryland, USA
09:50-10:15	Tianjun Zhou	The Paris Agreement and climate change over global monsoon regions
		Professor, Institute of Atmospheric Physics, Chinese Academy of Sciences (CAS); Deputy Director, CAS Center for Climate Change Research, China
10:15-10:45	Coffee & Tea Break	
Chair: Xiaoming WANG Professor, State Key Laboratory of Cryospheric Science, CAS, China		
10:45-11:10	Shilu Tong	Quantifying Health Risks of Climate Change: Advances and Challenges
		Professor, Children's Medical Center, Shanghai Jiao Tong University, China; Professor, Queensland University of Technology, Australia
11:10-11:35	Patrick Kinney	Health Benefits of Urban Climate Mitigation Actions
		Professor, Department of Environmental Health, School of Public Health, Boston University, USA
11:35-12:00	Virginia Murray	How can the Global Heat Health Information Network (GHHIN) assist in reducing the health impacts of extreme heat and rising temperatures?
		Head of Global Disaster Risk Reduction for Public Health England, UK
12:00-14:00	Lunch	
Sunday Afternoon, 2nd December 2018		
SESSION 1: Protecting Health in One Atmosphere		
Chair: Cunrui HUANG Professor, School of Public Health, Sun Yat-sen University, China		
14:00-14:20	Bin Jalaludin	Air Pollution and Climate Change: The Connections
		Manager, South Western Sydney Local Health District; Conjoint Professor, University of New South Wale, Australia
14:20-14:40	Xuemei Wang	Numerical Simulation of Fine Urban Atmospheric Environment and Health Exposure
		Professor and Associate Dean of Institute of Environment and Climate, Jinan University, China
14:40-15:00	Yun-Chul Hong	New Findings on Temperature Effect and Attributable Deaths to Heatwave in Korea
		Professor and Director, Department of Preventive Medicine, Seoul National University, Korea
15:00-15:20	Haidong Kan	Ambient Temperature and Mortality Risk and Burden in China
		Professor and Associate Dean of School of Public Health, Fudan University, China
15:20-15:40	Linwei Tian	Weather as a Trigger of Stroke
		Associate Professor, School of Public Health,

		The University of Hong Kong, China
15:40-16:00	Coffee & Tea Break	
SESSION 2: Enhancing Research Evidence in the Asia Pacific Region		
Chair: Cordia CHU Professor, Director of Centre for Environment and Population Health, Griffith University, Australia		
16:00-16:10	Xiaoming Wang	Issues in Development and Implementation of Climate Change Adaptation Policies
		Professor, State Key Laboratory of Cryospheric Science, CAS, China; Senior Principal Scientist, CSIRO, Australia
16:10-16:20	Jamal Hisham Hashim	Health Impacts of Climate Change in Southeast Asia
		Visiting Professor, United Nations University- Institute for Global Health, UKM Medical Centre, Malaysia
16:20-16:30	Biraj Karmacharya	Role of Universities in Addressing Climate Change and Health
		Chief, Department of Community Programs, *Dhulikhel Hospital-Kathmandu University Hospital, Nepal*
16:30-16:40	Mohammad Sohel Shomik	Generating Evidence for Impact of Climate Change on Tropical Diseases and Nutrition in Bangladesh
		Deputy Project Coordinator, International Centre for *Diarrhoeal Disease Research (ICDDR), Bangladesh*
16:40-16:50	Tran Ngoc Dang	The Impact of Temperature on Mortality and Hospitalization and the Readiness of Health Science Students for Climate Change Responses in Vietnam
		Lecturer, Department of Environmental Health, *University of Medicine and Pharmacy at Ho Chi Minh City, Vietnam*
16:50-17:00	Santosh Kumar	Influences of Climate Change in Kumaun Himalaya: A Case Study of Pindari Region
		Assistant Professor, Department of Geography, *University of Delhi, India*
17:00-17:30	**Panel Discussion** (Panelists: Xiaoming Wang, Jamal Hisham Hashim, Biraj Karmacharya, Mohammad Sohel Shomik, Tran Ngoc Dang, Santosh Kumar)	
18:30-20:00	Dinner	
Monday Morning, 3rd December 2018		
SESSION 3: Climate Variables, Health Effects and Labor Productivity		
Chair: Yaodong DU Professor and Technical Chief of Guangdong Meteorological Bureau, China		

9:00-9:20	Marco Morabito	The HEAT-SHIELD Personalized Warning System for European Workers and Other Adaptation Solutions to Minimize Detrimental Health and Productivity Effects of Workers Caused by Global Warming
		Researcher, Institute of Biometeorology, National Research Council, Italy
9:20-9:40	Chuansi Gao	Extreme Weather Events, Human Heat Balance, Thermal Stress Warnings and Advice through a Smart Phone (ClimApp)
		Associate Professor, Faculty of Engineering, Lund University, Sweden
9:40-10:00	Ho Kim	Introducing MOTIVE (Model of Integrated Impact and Vulnerability Evaluation of climate change) of Korea
		Professor, Dean of Graduate School of Public Health, Seoul National University, Korea
10:00-10:20	Amir Sapkota	Attributes of Changing Climate and Impaired Health: Local to Global Perspectives
		Associate Professor, School of Public Health, University of Maryland, USA
10:20-10:40	Coffee & Tea Break	
SESSION 4: Innovative Research Design and Modelling Approaches		
Chair: Shilu TONG Professor, School of Public Health, Queensland University of Technology, Australia		
10:40-11:00	Xin-Zhong Liang	Prediction and Identification of Extreme Weather and Air Quality Events for Health Effects
		Professor, The Earth System Model Research and Development Laboratory, University of Maryland, USA
11:00-11:20	Luke Knibbs	New Research Methods for Tackling Old and Emerging Environmental Health Challenges
		Senior Lecturer, School of Public Health, The University of Queensland, Australia
11:20-11:40	Yuqiang Zhang	Co-benefits of Global and Regional GHGs Mitigation on Global and Regional Air Quality and Human Health
		Research Scientist, Nicholas School of the Environment, Duke University, USA
11:40-12:00	Sindana Ilango	Climate Change and Aging: Methods to link existing datasets and address inferential challenges in ageing research
		PhD Student, Department of Family Medicine and Public Health, University of California, San Diego, USA
12:00-14:00	Lunch	


2nd INTERNATIONAL FORUM ON
CLIMATE CHANGE AND HEALTH RESPONSE
UNDER THE "BELT & ROAD" INITIATIVE
第2届“一带一路”气候变化与健康应对国际论坛
DECEMBER 2nd – 4th, 2018
2018年12月2 – 4日


2nd INTERNATIONAL FORUM ON
CLIMATE CHANGE AND HEALTH RESPONSE
UNDER THE "BELT & ROAD" INITIATIVE
第2届“一带一路”气候变化与健康应对国际论坛
GUANGZHOU, CHINA DECEMBER 2nd – 4th, 2018