Who is more Vulnerable to Death from Extremely Cold Temperatures? A Case-Only Approach in Hong Kong with a Temperate Climate

Hong Qiu [a], Linwei Tian [a]*, Kin-fai Ho [b], Ignatius T.S. Yu [c], Thuan-Quoc Thach [a], Chit-Ming Wong [a]

[a]: School of Public Health, Li Ka Shing Faculty of Medicine, The University of Hong Kong. [b]:The Jockey Club School of Public Health and Primary Care, The Chinese University of Hong Kong. [c]: Hong Kong Occupational and Environmental Health Academy.

Type of manuscript: Original Article

Running Title: Effect Modification on Extreme Cold Associated Mortality

*** Corresponding author:**

Dr. Linwei Tian, School of Public Health, Li Ka Shing Faculty of Medicine, The University of Hong Kong, 21 Sassoon Road, Pokfulam, Hong Kong. Phone: (+852)2831 5071; Fax: (+852) 2855 9528 Email: linweit@hku.hk.

The authors declare that they have no competing interests.

Funding support: None

Key Words:

Case-Only Study; Cause of Death; Effect Modifiers; Extreme Cold; Mortality

Acknowledgements:

The authors thank the Census and Statistical Department of Hong Kong for providing mortality data, the Hong Kong Observatory for providing temperature data, and the Hong Kong Environmental Protection Department for providing air pollution data.

Authors' contributions:

HQ, LWT, and ITY defined the research theme. HQ, LWT and KFH analyzed the data, interpreted the results and wrote the paper. TQT and CMW co-worked on associated data collection and their interpretation.

Abstract

Short-term effects of ambient cold temperature on mortality have been well documented in the literature worldwide. However, less is known about which subpopulations are more vulnerable to death related to extreme cold. We aimed to examine the personal characteristics and underlying causes of death that modified the association between extreme cold and mortality in a case-only approach. Individual information of 197,680 deaths of natural causes, daily temperature and air pollution concentrations in cool season (November ~ April) during 2002 - 2011 in Hong Kong were collected. The extreme cold was defined as those days with preceding week with a daily maximum temperature at or less than the 1st percentile of its distribution. Logistic regression models were used to estimate the effects of modification, further controlling for age, seasonal pattern and air pollution. Sensitivity analyses were conducted by using the 5th percentile as cutoff point to define the extreme cold. Subjects with age of 85 and older were more vulnerable to extreme cold, with odds ratio (OR) of 1.33 (95%CI: 1.22-1.45). The greater risk of extreme cold related mortality was observed for total cardiorespiratory diseases and several specific causes including hypertensive diseases, stroke, congestive heart failure, COPD and pneumonia. Hypertensive diseases exhibited the greatest vulnerability to extreme cold exposure, with OR of 1.37 (95%CI: 1.13-1.65). Sensitivity analyses showed the robustness of these effect modifications. This evidence on which sub-populations are vulnerable to the adverse effects of extreme cold is important to inform public health measures to minimize those effects.

Key Words:

Case-Only Study; Cause of Death; Effect Modifiers; Extreme Cold; Mortality

Introduction

Studies on the associations between extreme cold/hot temperatures and daily mortality have been well documented in the literature (Curriero et al. 2002; Hajat et al. 2007; Analitis et al. 2008; Basagaña et al. 2011; Chen et al. 2013; Guo et al. 2014). Researchers have found that both cold and hot temperatures are associated with increased risk of mortality. In general, cold effects are delayed and last for more than a few days, whereas heat effects appear quickly and do not last long. At the same time, identification of factors that modify the effects of extreme temperatures on mortality is also an issue of interest in the scientific community. A greater susceptibility has been reported for the elderly and female (Hajat et al. 2007; Analitis et al. 2008; Zhou et al. 2014; Zeng et al. 2014), and for those with lower socioeconomic status (Armstrong 2003; Hajat et al. 2007; Xu et al. 2013). Regarding the medical conditions and preexisting diseases that may confer susceptibility, results of previous studies from different regions are geographically heterogeneous (Schwartz 2005; Medina-Ramón et al. 2006; Madrigano et al. 2013; Zanobetti et al. 2013; Zhou et al. 2014).

Hong Kong is a subtropical city located on the southern coast of China, with hot summer and milder winter. The associations of extremely cold and hot temperatures with the increased risk of mortality (Chan et al. 2012; Goggins et al. 2013; Yi and Chan 2015) have been studied. Authors found the heat-related mortality varied with sociodemographic characteristics (Chan et al. 2012), and the cold-related mortality was greater among elders and non-cancer patients (Goggins et al. 2013). However in these studies, researchers used time series Poisson model to estimate the main temperature effect and stratified subgroup analyses to access the potential modification, where the comparisons among subgroups were not conducted and the statistical power might have been reduced. As an alternative, Armstrong BG in 2003 firstly proposed and applied the case-only approach to access how the fixed factors modified the effects of time varying factors in time series study (Armstrong 2003). Being a simplified approach that reduces the vulnerability to model miss-specification bias (Armstrong 2003; Zanobetti et al. 2013), case-only analysis has its advantages over the conventional time series analysis on assessing the effect modification.

A greater effect of colder temperatures on mortality risk has been suggested in cities with warmer winter (Curriero et al. 2002; Analitis et al. 2008), and studies conducted in warmer areas with higher long-term mean temperatures tended more frequently to report detrimental effects of cold (Bhaskaran et al. 2009). Hong Kong has hot summer and temperate winter, with very high prevalence of air conditioner usage in summer but almost no house heating in winter, so that the subjects might be more vulnerable to cold. Identifying the most susceptible subpopulations would have great public health implications in this region. In the current study, we aimed to use a case-only approach to identify the time invariant individual factors that confer susceptibility to extreme cold associated mortality, including personal social-demographic characteristics and specific causes of death.

Materials and Methods

Mortality Data

Daily mortality data during the cool seasons (November-April) in 2002-2011 were obtained from Census and Statistical Department of Hong Kong. Individual information included personal characteristics such as age, sex, occupational status and marital status. Primary causes of death were coded in *International Classification of Diseases, 10th version*. The underlying causes of death examined in this study as potential modifiers included all diseases of circulatory system (ICD-10: I00-I99), diseases of respiratory system (ICD-10: J00-J99) and diabetes (ICD-10: E10-E14). Some specific causes of cardiorespiratory death were also examined, including stroke (ICD-10: I60-I69), hypertensive diseases (HBP, ICD-10: I10-I15), myocardial infarction (MI, ICD-10: I21, I22), congestive heart failure (CHF, ICD-10: I50), cardiac arrest (ICD-10: I46), chronic obstructive pulmonary disease (COPD, ICD-10: J40-J44, J47) and pneumonia (ICD-10: J12-J18).

Temperature and Air Pollution Data

The daily minimum, mean and maximum temperature from 2002 to 2011 was obtained from the Hong Kong Observatory. The extremely cold days were defined as those days with preceding week with a daily maximum temperature at or less than the 1st percentile of its distribution in Hong Kong (Medina-Ramón et al. 2006). The calculation was based on the temperature on the 7-day moving average of the day of death and the 6 preceding days (lag06), as previous studies have suggested that mortality is more related to days following a several days with on average low temperature than to a single day of cold (Saez et al. 1995), and the cold effect would last for longer days than hot effect (Guo et al. 2014). Different cutoff point using daily maximum temperature at or less than the 5th percentile to define the extremely cold days was also tried in the sensitivity analyses.

Air pollution concentrations in the same period were obtained from the Environmental Protection Department of Hong Kong. We calculated the daily 24-hr mean concentrations of PM_{10} and NO_2, and daytime 8-hr (10:00-17:00) mean concentrations of O_3 for each general monitoring, and then averaged them across the ten stations (Qiu et al. 2013). Air pollutants would be acted as potential confounders in the data analysis.

Analytic Method

This is a case-only approach to assess how the association between extreme temperature and mortality was modified by the personal characteristics and the specific primary causes of death. The underlying idea behind this approach is that if a time invariant factor increases the risk of dying on extremely cold (or hot) days, a greater proportion of people who died during those periods would be expected to have this factor, compared with people who died during milder weather conditions. Hence, if a characteristic is a risk modifier for deaths during extremely cold days, then extreme cold exposure should be a predictor of the occurrence of that characteristic on death certificates using logistic regression. Formal proof of the approach was provided by Armstrong (Armstrong 2003). Several studies followed this approach to identify the sensitive subpopulation who is more vulnerable to die from extreme temperatures (Schwartz 2005; Medina-Ramón et al. 2006; Medina-Ramón and Schwartz 2007; Zanobetti et al. 2013).

The validity of this approach depends on the assumption that the modifier and exposure are independent, that is, not associated in the base population that gave rise to the deaths. Because the personal characteristics vary among individuals but not fluctuate from day to day variation of temperature, this assumption is clearly met in studies of ambient temperature. Armstrong also suggested that the assumption that modifiers are fixed in time could be relaxed to allow modifiers that change in time much more slowly than does the temperature, such as age, chronic diseases, and some long-term treatments (Armstrong 2003). The case-only approach was proposed to analyze the effect modification but not the main effect, and the motivation is simplification of modeling and reduced vulnerability to model miss-specification bias.

As the personal characteristics such as gender, non-married marital status, and economically inactive were all associated with old age, and Armstrong noted that "Interaction of the time-varying factor of interest with another time-fixed variable" was "almost certain to confound" an interaction of interest in a case-only analysis, we tried the analyses by including the potential confounding of age as a four-level categorical variable (age<65, age of 65-74, age of 75-84 and age>=85) in order to get the age-controlled estimates of modification. Considering the possible interaction of the putative modifier under investigation with other time-varying factors such as air pollutants, which would confound the modification of interest (Armstrong 2003), we also did sensitivity analysis by including air pollutants (PM_{10}, NO_2 and O_3) as additional indicators in the logistic regression model. Furthermore, because of the baseline seasonal pattern of mortality, the additional non-temperature related modifiers of risk by predisposing condition might be captured by a sine and cosine term with 365.24-day period (Schwartz 2005). We therefore included an annual sine-cosine pair to sufficiently control for a seasonal component that might plausibly confound the modifier of interest and extreme temperature.

Binary logistic regression was repeatedly used to examine the modifier with two levels such as personal characteristics (gender, employment and marital status); multinomial logistic regression was used to examine the modifier with several categories such as age and specific causes of death. All analyses were conducted in SPSS version 20.0.

Results

We included a total of 197,680 natural causes of death in cool seasons in Hong Kong in this case-only analysis. Most of deaths were age of 75 years and older (62.6%), and males (55.4%), and around half were married (47.4%). The majority of the deaths was economically inactive (90.7%). Diseases of circulatory and respiratory system accounted for 28.8% and 20.4% of the total natural causes of death, respectively (Table-1). The temporal distribution of daily minimum/mean/maximum temperature from 2002 to 2011 was displayed in time-series plots (Figure-1). The cutoff point used to define the extremely cold days was 14.7°C for the maximum temperature of 7-day moving average (lag06), the 1st percentile of its distribution during the study period.

Table-2 shows the individual characteristics that modify the extremely cold temperature related mortality. People aged >=75 years (compared with 'age<65yrs'), females (compared with 'males'), those economically inactive (compared with 'with occupation'), and those never married/widowed/divorced (compared with 'married') showed larger risk estimates of extreme cold, with ORs of 1.06-1.33 for extreme cold. However, the age-controlled estimates of modification for 'female', 'economically inactive' and 'never married/widowed/divorced' decreased and lost statistical significance, which may probably be due to their association with old age. Causes of cardiorespiratory diseases (compared with other natural causes) had higher risks of death related to extremely cold temperature, with OR of 1.17 (95%CI: 1.10-1.25) for total circulatory diseases and 1.13 (95%CI: 1.05-1.22) for total respiratory diseases, respectively. Among the specific causes of death, COPD, pneumonia, stroke, hypertensive diseases, and congestive heart failure showed greater susceptibility to death on days following extremely cold periods (Table-3). The greatest risk of cold related mortality was observed for hypertensive diseases, with OR of 1.37 (95%CI: 1.13-1.65). The modifications of the specific circulatory causes on cold related mortality were robust after controlling for age, seasonal pattern (a sine and cosine term with 365.24-day period) and air pollutants (PM_{10}, NO_2 and O_3).

Sensitivity analyses using the 5^{th} percentile as the cutoff point to define the extremely cold days got similar estimates, which appeared to result in a larger statistical power to capture more personal characteristics and specific causes of death including diabetes and MI as the modifiers for the cold associated mortality (Table-4).

Discussion

In this case-only study conducted in cool seasons in Hong Kong, we identified several sub-populations that are particularly susceptible to extremely cold temperatures. Subjects with hypertensive diseases were especially vulnerable to extreme cold. The increase in deaths on days following extremely cold periods was higher also for stroke, MI, CHF, COPD and pneumonia. Among the personal characteristics, only older age was clearly associated with elevated risk of mortality from extremely cold temperatures.

Chronic Diseases. It is explicable that subjects with hypertensive diseases show the greatest susceptibility to the effects of extremely cold temperature. Cold stress has been found to result in raising blood pressure, increasing the blood viscosity and platelet counts (Keatinge et al. 1984; Elwood et al. 1993). The cold effects on homeostasis system with increased fibrinogen, together with the effect on blood pressure, could explain a large part of the increase in myocardial infarction in the winter (Elwood et al. 1993). The marked increase of deaths from stroke on extremely cold days may also relate to the higher blood pressure in winter and increased levels of plasma cholesterol and fibrinogen (Keatinge et al. 1984; Fröhlich et al. 1997) which could facilitate the formation of blood clots and lead to thrombosis through haemoconcentration. It is interesting we found the higher risk of dying from congestive heart failure on days following extremely cold periods, which was not reported in previous studies (Schwartz 2005; Medina-Ramón et al. 2006). Congestive heart failure would be a result of many cardiovascular diseases or occur when several cardiovascular diseases/conditions are present at once. However, we did not found the increased vulnerability for cardiac arrest on extremely cold days as a previous study reported (Medina-Ramón et al. 2006), which could result from the small sample size in our study. We only recorded 284 cardiac arrest cases during the ten years' study period, accounting for 0.1 percent of the total deaths.

The increased susceptibility of causes of respiratory diseases especially COPD and pneumonia are also noteworthy. The lungs of persons with COPD and pneumonia are typically colonized by bacteria, and cold weather can easily exacerbate respiratory infections (Burge 2006). In addition, cold can induce bronchospasm, as well as increase platelet and red cell counts, and blood viscosity (Keatinge et al. 1984). Because persons with COPD often have cardiovascular complications, these effects on blood components may also play a role.

Sociodemographic Factors. Being consistent with the previous studies (Schwartz 2005; Hajat et al. 2007; Analitis et al. 2008; Medina-Ramón and Schwartz 2008; Zhou et al. 2014; Yi and Chan 2015), we found a greater susceptibility of the elderly to extreme cold related death. A reduced thermoregulatory capacity in the elderly, combined with a diminished ability to detect changes in their body temperature, may partly explain their increased susceptibility. A French three-city study found that outdoor temperature and blood pressure are strongly correlated in the elderly (Alpérovitch et al. 2009). The elderly may also have a higher prevalence of co-morbidities which would make them more sensitive to cold effect.

The modification effects of other personal characteristics including 'female', 'economically inactive' and 'never married/widowed/divorced' were less significant and less robust, and the age-controlled estimates of modification disappeared. These characteristics and old age were interrelated, so that their vulnerability may probably be explained by old age. The susceptibility of females may be due to the fact that they live longer. The susceptibility of those economically inactive may be due to the group of retired and again be explained by age; and the susceptibility of those never married/widowed/divorced may be driven by the widowed group and therefore be explained by age (or sex).

Advantages of case-only approach. The conventional approach to investigate the modification of personal characteristics and pre-existing comorbidities is by inclusion of interaction terms in the regression model of outcome on the exposure and modifier, or by carrying out separate regressions on strata with different modifier status (Lipsett et al. 1997; Zanobetti et al. 2000; Zeka et al. 2006; Peel et al. 2007; Kan et al. 2008; Qian et al. 2013). However, the case-only approach provides important advantages over traditional analyses in examining the effect modification, including reduction of potential confounding by variables typically associated with mortality, simplification of modeling, and reduction of results sensitivity to model misspecification bias (Armstrong 2003; Zanobetti et al. 2013). Of particular interest, the long term trend and periodicity in mortality whose modeling is quite complex, drops out in case-only approach. It was encouraging that in this study, seasonal pattern and air pollutants did not appear to confound the modification of interested factors. Using the 5th percentile as the cutoff point to define the extremely cold days seemed easier to identify the specific cardiorespiratory causes of death as the modifiers for the cold associated mortality, which may be due to the larger statistical power than the 1st percentile being used as the cutoff. Although such findings need to be confirmed in more locations, including areas with different climates, they support the use of the case-only approach to examine susceptibility.

Limitations of this study. One limitation of this study is that we could not link the death data to the previous medical records of the decedents, so that we were unable to abstract the pre-existing comorbidities for each subject. Although the subjects who died of cardiorespiratory diseases might have had pre-existing chronic cardiorespiratory diseases, modification of the specific primary causes of death identified in this study could not exactly represent the modification of the pre-existing comorbidities. Second, air pollution concentrations averaged from general monitoring stations were assigned to all the decedents. This may introduce some misclassification of the pollution exposure although the potential error can be non-differential. Another limitation came from the case-only study design itself, which cannot estimate the main effect of the extreme cold but only the effect modification by certain characteristics. With the main effects of cold temperature on mortality in Hong Kong been well studied previously (Goggins et al. 2013; Guo et al. 2014; Yi and Chan 2015), however, examining the effect modification was the main purpose of the current study.

Conclusions

We identified old age and some specific cardiorespiratory causes including hypertensive diseases, stroke, congestive heart failure, COPD and pneumonia that are particularly susceptible to extreme cold related mortality. Understanding who is susceptible to the extreme events will be important in minimizing their public health impact. The vulnerable subpopulations identified in this study may use central heating to mitigate the cold effect on days following extremely cold periods.

References:

Alpérovitch A, Lacombe J, Hanon O, et al (2009) Relationship Between Blood Pressure and Outdoor Temperature in a Large Sample of Elderly Individuals: The Three-City Study. Arch Intern Med 169:75–80.

Analitis A, Katsouyanni K, Biggeri A, et al (2008) Effects of cold weather on mortality: Results from 15 European cities within the PHEWE project. Am J Epidemiol 168:1397–1408.

Armstrong BG (2003) Fixed factors that modify the effects of time-varying factors: applying the case-only approach. Epidemiology 14:467–72.

Basagaña X, Sartini C, Barrera-Gómez J, et al (2011) Heat waves and cause-specific mortality at all ages. Epidemiology 22:765–72.

Bhaskaran K, Hajat S, Haines a, et al (2009) Effects of ambient temperature on the incidence of myocardial infarction. Heart 95:1760–9.

Burge P (2006) Prevention of exacerbations: how are we doing and can we do better? Proc Am Thorac Soc 3:257–61.

Chan EYY, Goggins WB, Kim JJ, Griffiths SM (2012) A study of intracity variation of temperature-related mortality and socioeconomic status among the Chinese population in Hong Kong. J Epidemiol Community Health 66:322–7.

Chen R, Wang C, Meng X, et al (2013) Both low and high temperature may increase the risk of stroke mortality. Neurology 81:1064–70.

Curriero FC, Heiner KS, Samet JM, et al (2002) Temperature and mortality in 11 cities of the eastern United States. Am J Epidemiol 155:80–7.

Elwood PC, Beswick A, Brien JRO, et al (1993) Temperature and risk factors for ischaemic heart disease in the Caerphilly prospective study. Br Heart J 70:520–523.

Fröhlich M, Sund M, Russ S, et al (1997) Seasonal variations of rheological and hemostatic parameters and acute-phase reactants in young, healthy subjects. Arterioscler Thromb Vasc Biol 17:2692–2697.

Goggins WB, Chan EYY, Yang C, Chong M (2013) Associations between mortality and meteorological and pollutant variables during the cool season in two Asian cities with sub-tropical climates: Hong Kong and Taipei. Environ Health 12:59.

Guo Y, Gasparrini A, Armstrong B, et al (2014) Global variation in the effects of ambient temperature on mortality: a systematic evaluation. Epidemiology 25:781–9.

Hajat S, Kovats RS, Lachowycz K (2007) Heat-related and cold-related deaths in England and Wales: who is at risk? Occup Environ Med 64:93–100.

Kan H, London SJ, Chen G, et al (2008) Season, sex, age, and education as modifiers of the effects of outdoor air pollution on daily mortality in Shanghai, China: The Public Health and Air Pollution in Asia (PAPA) Study. Environ Health Perspect 116:1183–8.

Keatinge WR, Coleshaw SRK, Cotter F, et al (1984) Increases in platelet and red cell counts , blood viscosity , and arterial pressure during mild surface cooling : factors in mortality from coronary and cerebral thrombosis in winter. Br Med J 289:1405–8.

Lipsett M, Hurley S, Ostro B (1997) Air pollution and emergency room visits for asthma in Santa Clara County, California. Environ Health Perspect 105:216–22.

Madrigano J, Mittleman M a, Baccarelli A, et al (2013) Temperature, myocardial infarction, and mortality: effect modification by individual- and area-level characteristics. Epidemiology 24:439–46.

Medina-Ramón M, Schwartz J (2007) Temperature, temperature extremes, and mortality: a study of acclimatisation and effect modification in 50 US cities. Occup Environ Med 64:827–33.

Medina-Ramón M, Schwartz J (2008) Who is more vulnerable to die from ozone air pollution? Epidemiology 19:672–9.

Medina-Ramón M, Zanobetti A, Cavanagh DP, Schwartz J (2006) Extreme Temperatures and Mortality: Assessing Effect Modification by Personal Characteristics and Specific Cause of Death in a Multi-City Case-Only Analysis. Environ Health Perspect 114:1331–1336.

Peel JL, Metzger KB, Klein M, et al (2007) Ambient air pollution and cardiovascular emergency department visits in potentially sensitive groups. Am J Epidemiol 165:625–33.

Qian Y, Zhu M, Cai B, et al (2013) Epidemiological evidence on association between ambient air pollution and stroke mortality. J Epidemiol Community Health 67:635–40.

Qiu H, Yu IT-S, Wang X, et al (2013) Cool and dry weather enhances the effects of air pollution on emergency IHD hospital admissions. Int J Cardiol 168:500–5.

Saez M, Sunyer J, Castellsague J, Murillo C (1995) Relationship between Weather Temperature and Mortality : A Time Series Analysis Approach in Barcelona. Int J Epidemiol 24:576–582.

Schwartz J (2005) Who is Sensitive to Extremes of Temperature? Epidemiology 16:67–72.

Xu Y, Dadvand P, Barrera-Gómez J, et al (2013) Differences on the effect of heat waves on mortality by sociodemographic and urban landscape characteristics. J Epidemiol Community Health 67:519–25.

Yi W, Chan APC (2015) Effects of temperature on mortality in Hong Kong: a time series analysis. Int J Biometeorol 59:927–936.

Zanobetti a, Schwartz J, Gold D (2000) Are there sensitive subgroups for the effects of airborne particles? Environ Health Perspect 108:841–5.

Zanobetti A, O’Neill MS, Gronlund CJ, Schwartz JD (2013) Susceptibility to mortality in weather extremes: effect modification by personal and small-area characteristics. Epidemiology 24:809–19.

Zeka A, Zanobetti A, Schwartz J (2006) Individual-level modifiers of the effects of particulate matter on daily mortality. Am J Epidemiol 163:849–59.

Zeng W, Lao X, Rutherford S, et al (2014) The effect of heat waves on mortality and effect modifiers in four communities of Guangdong Province, China. Sci Total Environ 482-483:214–21.

Zhou MG, Wang LJ, Liu T, et al (2014) Health impact of the 2008 cold spell on mortality in subtropical China: the climate and health impact national assessment study (CHINAs). Environ Health 13:60.

Table-1 Descriptive Statistics for Natural Causes of Death in Cool Seasons in Hong Kong (November-April, 2002-2011)

Category	Number	Percentage (%)
Total	197,680	100.0
Age		
<65 yrs	36,570	18.5
65-74 yrs	37,425	18.9
75-84 yrs	66,103	33.4
>=85 yrs	57,582	29.1
Sex		
Male	109,505	55.4
Female	88,175	44.6
Occupational Status		
With occupation	18,402	9.3
Economically inactive	179,278	90.7
Married Status		
Married	93,775	47.4
Never married/Widowed/Divorced	75,585	38.2
Unknown	28,320	14.3
Cause of death		
Diabetes	3,209	1.6
All cardiovascular diseases	57,024	28.8
Stroke	18,657	9.4
Hypertensive Diseases	3,720	1.9
Myocardial Infarction	10,550	5.3
Congestive Heart Failure	4,283	2.2
Cardiac Arrest	158	0.1
All respiratory diseases	40,310	20.4
COPD	10,092	5.1
Pneumonia	25,808	13.1

Figure-1 The temporal distribution of daily maximum/mean/minimum temperature (°C) in Hong Kong, 2002-2011

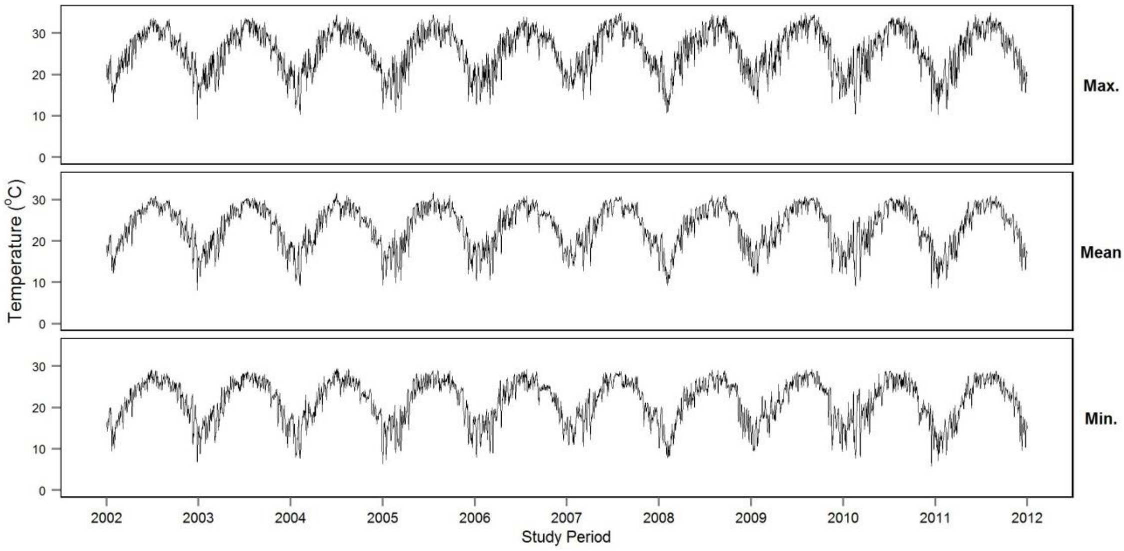

Table-2 Modification by Personal Characteristics of the Effect of Extremely Cold Temperatures on Mortality in Cool Seasons in Hong Kong, 2002-2011 (OR (95%CI))*

Characteristics	Model 1 [a]	Model 2 [b]	Model 3 [c]
Age of 65-74yrs	1.05 (0.95, 1.15)	-	1.04 (0.95, 1.15)
Age of 75-84yrs	**1.19 (1.10, 1.30)**	-	**1.19 (1.10, 1.30)**
Age of 85yrs and older	**1.33 (1.22, 1.45)**	-	**1.33 (1.22, 1.45)**
Female	**1.06 (1.00, 1.12)**	1.01 (0.96, 1.07)	**1.06 (1.00, 1.12)**
Economically Inactive	**1.11 (1.00, 1.23)**	1.02 (0.92, 1.14)	1.09 (0.98, 1.20)
Never married/Widowed /Divorced	**1.08 (1.01, 1.15)**	1.02 (0.96, 1.09)	**1.08 (1.01, 1.15)**

*: Estimates represent the ratio of relative risk associated with extreme cold in persons who have the condition (e.g. being female) relative to that ratio in other persons. For the age groups, all compared with the age less than 65yrs group. The extremely cold days were defined as those with a daily maximum temperature at or less than the 1st percentile of its distribution in Hong Kong during 2002-2011, based on the temperature on the 7-day moving average of same day of death and the 6 preceding days.
[a]: single factor model with extreme cold only; [b]: model 1 further controlling for confounding from age as a four-level categorical factor; [c]: model 1 further controlling for confounding from seasonal pattern (captured by an annual sine-cosine pair with 365.24-day period) and air pollutants (PM_{10}, NO_2 and O_3).

Table-3 Primary Causes of Death as Modifiers of the Effect of Extremely Cold Temperatures on Mortality in Cool Seasons in Hong Kong, 2002-2011 (OR (95%CI))*

Cause of Death	Model 1 [a]	Model 2 [b]	Model 3 [c]
Diabetes	1.19 (0.96, 1.48)	1.17 (0.94, 1.45)	1.19 (0.96, 1.48)
All Circulatory Diseases	**1.17 (1.10, 1.25)**	**1.13 (1.06, 1.21)**	**1.17 (1.10, 1.25)**
Stroke	**1.14 (1.03, 1.26)**	**1.10 (1.00, 1.22)**	**1.14 (1.03, 1.26)**
Hypertensive Diseases	**1.37 (1.13, 1.65)**	**1.31 (1.08, 1.58)**	**1.37 (1.13, 1.66)**
Myocardial Infarction	1.09 (0.96, 1.24)	1.07 (0.94, 1.21)	1.09 (0.96, 1.24)
Congestive Heart Failure	**1.25 (1.04, 1.50)**	1.16 (0.96, 1.39)	**1.25 (1.04, 1.50)**
Cardiac Arrest	1.10 (0.41, 2.96)	1.06 (0.39, 2.87)	1.02 (0.38, 2.77)
All Respiratory Diseases	**1.13 (1.05, 1.22)**	1.06 (0.99, 1.15)	**1.13 (1.05, 1.22)**
COPD	**1.14 (1.00, 1.29)**	1.09 (0.95, 1.24)	1.12 (0.99, 1.28)
Pneumonia	**1.16 (1.06, 1.26)**	1.08 (0.98, 1.18)	**1.16 (1.06, 1.26)**

*: Estimates represent the ratio of relative risk associated with extreme cold in persons who die from a specific cause of death (e.g. stroke) relative to that ratio in persons dying from other non-cardiorespiratory and non-diabetes causes. The extremely cold days were defined as those with a daily maximum temperature at or less than the 1st percentile of its distribution in Hong Kong during 2002-2011, based on the temperature on the 7-day moving average of same day of death and the 6 preceding days.
[a]: single factor model with extreme cold only; [b]: model 1 further controlling for confounding from age as a four-level categorical factor; [c]: model 1 further controlling for confounding from seasonal pattern (captured by an annual sine-cosine pair with 365.24-day period) and air pollutants (PM_{10}, NO_2 and O_3).

Table-4 Sensitivity Analysis using the 5th percentile as the cutoff to define the extreme cold (OR (95%CI))*

Condition	Model 1 [a]	Model 2 [b]	Model 3 [c]
Characteristics			
Age of 65-74yrs	1.01 (0.97, 1.06)	-	1.00 (0.96, 1.05)
Age of 75-84yrs	**1.08 (1.04, 1.13)**	-	**1.08 (1.04, 1.13)**
Age of 85yrs and older	**1.17 (1.12, 1.22)**	-	**1.17 (1.13, 1.22)**
Female	**1.03 (1.00, 1.06)**	1.00 (0.97, 1.03)	**1.03 (1.00, 1.06)**
Economically Inactive	1.01 (0.97, 1.06)	0.97 (0.92, 1.02)	0.98 (0.94, 1.03)
Never married/Widowed /Divorced	**1.06 (1.03, 1.09)**	1.02 (0.99, 1.06)	**1.06 (1.03, 1.10)**
Cause of death			
Diabetes	**1.20 (1.08, 1.33)**	**1.19 (1.07, 1.32)**	**1.17 (1.05, 1.30)**
All Circulatory Diseases	**1.17 (1.14, 1.21)**	**1.15 (1.12, 1.19)**	**1.16 (1.12, 1.20)**
Stroke	**1.16 (1.10, 1.21)**	**1.14 (1.09, 1.20)**	**1.15 (1.10, 1.21)**
Hypertensive Diseases	**1.31 (1.19, 1.44)**	**1.29 (1.17, 1.41)**	**1.30 (1.18, 1.44)**
Myocardial Infarction	**1.11 (1.04, 1.18)**	**1.10 (1.03, 1.17)**	**1.09 (1.02, 1.16)**
Congestive Heart Failure	**1.19 (1.09, 1.31)**	**1.15 (1.05, 1.26)**	**1.20 (1.09, 1.32)**
Cardiac Arrest	1.31 (0.83, 2.06)	1.29 (0.82, 2.03)	1.25 (0.79, 1.97)
All Respiratory Diseases	**1.11 (1.07, 1.15)**	**1.08 (1.04, 1.12)**	**1.11 (1.07, 1.16)**
COPD	**1.12 (1.05, 1.20)**	**1.10 (1.03, 1.17)**	**1.11 (1.04, 1.18)**
Pneumonia	**1.12 (1.07, 1.17)**	**1.08 (1.03, 1.13)**	**1.13 (1.09, 1.18)**

*: Estimates represent the ratio of relative risk associated with extreme cold in persons with sociodemographic characteristic or dying from a specific cause of death relative to that ratio in other persons. The extremely cold days were defined as those with a daily maximum temperature at or less than the 5th percentile of its distribution in Hong Kong during 2002-2011, based on the temperature on the 7-day moving average of same day of death and the 6 preceding days.

[a]: single factor model with extreme cold only; [b]: model 1 further controlling for confounding from age as a four-level categorical factor; [c]: model 1 further controlling for confounding from seasonal pattern (captured by an annual sine-cosine pair with 365.24-day period) and air pollutants (PM_{10}, NO_2 and O_3).