Increased susceptibility to heat for respiratory hospitalizations in Hong Kong

Shengzhi Sun\textsuperscript{a,b,1}, Wangnan Cao\textsuperscript{c,1}, Tonya G. Mason\textsuperscript{a}, Jinjun Ran\textsuperscript{a}, Hong Qiu\textsuperscript{a}, Jinhui Li\textsuperscript{a}, Yang Yang\textsuperscript{a}, Hualiang Lin\textsuperscript{d}, Linwei Tian\textsuperscript{a,*}

\textsuperscript{a} School of Public Health, The University of Hong Kong, Hong Kong, China
\textsuperscript{b} Department of Epidemiology, Brown University School of Public Health, Providence, RI, USA
\textsuperscript{c} Public Health and Healthy Ageing Research Group, Faculty of Dentistry, The University of Hong Kong, Hong Kong, China
\textsuperscript{d} Department of Medical Statistics and Epidemiology, School of Public Health, Sun Yat-sen University, Guangzhou, China

HIGHLIGHTS

\begin{itemize}
  \item Trends in temperature-respiratory hospitalization risks and AFs were assessed.
  \item Hong Kong people are more susceptible to heat but less susceptible to cold for RD.
  \item The overall temperature-related AFs for RD hospitalizations were generally constant.
\end{itemize}

GRAPHICAL ABSTRACT

ARTICLE INFO

Article history:
Received 19 November 2018
Received in revised form 13 January 2019
Accepted 15 February 2019
Available online 16 February 2019

Editor: SCOTT SHERIDAN

Keywords:
Respiratory disease
Extreme temperatures
Temporal change
Emergency department

ABSTRACT

Background: Emerging studies have shown temperature-mortality association is changing over time, but little is known about the temporal changes of the temperature-morbidity association.

Objectives: We aimed to evaluate the temporal variations in both temperature-respiratory hospitalizations associations and temperature-related attributable risks in Hong Kong.

Methods: We collected 17-year time-series data on daily ambient temperature and emergency hospital admissions for respiratory diseases between 2000 and 2016 in Hong Kong. Quasi-Poisson regression with a time-varying distributed lag nonlinear model was used to estimate the year-specific association between temperature and respiratory hospitalizations [total respiratory, pneumonia, and chronic obstructive pulmonary disease (COPD)] and the year-specific attributable fraction (AF) for heat and cold (defined as above/below the optimum temperature, respectively).

Results: Heat-related risks and AFs increased continuously for total respiratory, pneumonia and COPD hospitalizations during the past 17 years, respectively. Cold-hospitalization associations and cold-related AFs showed heterogeneous patterns, showing a decreasing trend for pneumonia but a general increasing trend for COPD for both the associations and AFs. The total temperature-related AFs remained stable for total respiratory (p for trend = 0.136) and pneumonia (p for trend = 0.406), but showed an increasing trend for COPD (p for trend < 0.001) from 10% (95% empirical CI: 2%, 17%) in 2000 to 17% (95% empirical CI: 11%, 22%) in 2016.

Conclusions: Our findings indicate an increased susceptibility to heat but a decreased susceptibility to cold for...
1. Introduction

Respiratory diseases impose an immense health burden worldwide. It is estimated that about 251 million people suffer from chronic obstructive pulmonary disease (COPD) (World Health Organisation, 2017a), and 235 million people have asthma (World Health Organisation, 2017b). According to the Global Burden of Diseases, Injuries, and Risk Factors 2016 study (Naghavi et al., 2017), over 3.5 million people died prematurely from chronic respiratory disease worldwide, 2.9 million from COPD, and 2.4 million from respiratory infection.

Prior studies suggested that extreme temperatures were associated with increased risks of respiratory morbidity and mortality (Anderson et al., 2013; Gasparini et al., 2013b; Michelozzi et al., 2009; Qiu et al., 2013; Sun et al., 2016; Sun et al., 2016; Sun et al., 2016; Tian et al., 2016). Since extreme temperatures have occurred more frequently in recent years, and are projected to further increase in frequency, intensity, and duration due to continued climate change (Pachauri et al., 2014; Sheridan and Allen, 2015). Thus, there is an urgent need to improve our prediction on the impact of temperature on respiratory diseases under climate change scenarios.

Prior studies mostly assumed a constant magnitude of the association between temperature and respiratory hospitalizations (Anderson et al., 2013; Qiu et al., 2016). However, the magnitude might be changing over time as suggested by emerging studies that reported temporal variations in associations of temperature with mortality (Chung et al., 2017; Diaz et al., 2018; Gasparini et al., 2015a; Gasparini et al., 2016; Lee et al., 2018a; Sheridan and Allen, 2018). For example, Gasparini et al. (2015a) conducted a multi-country time-series study used data from 272 locations from seven countries and found that the heat-related mortality risk decreased significantly in the majority of countries from 1993 to 2006 (Gasparini et al., 2015a). To our best knowledge, no study has evaluated whether there is a temporal trend in magnitude of the association between respiratory hospitalizations and ambient temperature.

Accordingly, we sought to examine whether there were temporal variations in the associations of ambient temperature with total respiratory, pneumonia, and COPD in Hong Kong between 2000 and 2016. To quantify the trend of hospitalization burden attributed to temperature, we also examined temporal trends in temperature-related attributable fraction for respiratory diseases.

2. Material and methods

2.1. Emergency respiratory diseases

The emergency hospital admissions for respiratory diseases between 2000 and 2016 were obtained from the Hospital Authority Corporate Data Warehouse. This Data Warehouse records hospital admissions from all publicly funded hospitals providing 24-hour emergency services, which covers a total of 90% hospital beds in Hong Kong (Tian et al., 2017). The data include age, sex, the exact date of admission, admission source through Accident & Emergency department (A&E), and principal diagnosis code for diseases. We restricted to emergency hospitalizations via A&E for respiratory diseases (ICD-9, principal discharge diagnosis codes: 460–519), pneumonia: 480–486 and 487.0, and COPD: 490–496. Daily hospitalizations were then aggregated by sex. As the data we used were aggregated and de-identified, ethical approval by the institutional review board was not required in this study.

2.2. Ambient temperature and air pollution data

We extracted daily mean ambient temperature and relative humidity between 2000 and 2016 from the Hong Kong Observatory. We defined extreme cold, moderate cold, moderate heat, and extreme heat as the 1st, 10th, 90th, and 99th percentile of the temperature distribution over the study period, respectively.

We collected air pollution data from ten general monitoring stations operated by the Hong Kong Environmental Protection Department (Supplemental Fig. S1). Air pollutants of interest included respirable particulate matter (PM$_{10}$), nitrogen dioxide (NO$_2$), and ozone (O$_3$). We calculated daily concentrations of air pollutants by averaging air pollutants across all eligible monitoring stations (Sun et al., 2015).

2.3. Statistical analysis

2.3.1. Trends in magnitude of the association

We estimated the time-varying association of ambient temperature with respiratory hospitalizations using a standard time-series quasi-Poisson regression incorporating a time-varying distributed-lag nonlinear model (DLNM) (Gasparrini, 2014). To control for seasonal and long-term trend, we included a natural cubic B-spline function with 8 degrees of freedom ($df$) per year in the model. We also controlled for day of the week, public holiday, relative humidity with a natural cubic B-spline with $3df$, and air pollution (i.e., PM$_{10}$, NO$_2$, and O$_3$). To describe the nonlinear and delayed temperature-hospitalizations association that changed over time, we included a time-varying DLNM in the model. Specifically, we first created a cross-basis term of temperature, which included a natural cubic B-spline for temperature with 3 internal knots placed at equal spaces in the temperature range and a natural cubic B-spline with 4 internal knots placed equally on the log scale of the lag day. We extended the lag day up to 21 to fully capture the delayed effects of temperature (Chen et al., 2018; Gasparini et al., 2015b; Guo et al., 2014; Tian et al., 2016). The selection of spline functions and knots was guided by the lowest quasi-Akaike score.

### Table 1

Summary statistics for daily emergency hospital admissions for respiratory diseases, air pollution, and weather conditions in Hong Kong, 2000–2016 ($n = 6210$ days).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean (SD)</th>
<th>Percentile</th>
<th>Min</th>
<th>25th</th>
<th>50th</th>
<th>75th</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily emergency hospital admissions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory diseases</td>
<td>264 (64)</td>
<td>89 220</td>
<td>254</td>
<td>297</td>
<td>563</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>157 (36)</td>
<td>48 132</td>
<td>152</td>
<td>176</td>
<td>320</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>107 (30)</td>
<td>35 85</td>
<td>101</td>
<td>123</td>
<td>269</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td>94 (46)</td>
<td>9 63</td>
<td>92</td>
<td>120</td>
<td>288</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>50 (24)</td>
<td>4 34</td>
<td>49</td>
<td>64</td>
<td>155</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>44 (23)</td>
<td>0 28</td>
<td>42</td>
<td>57</td>
<td>155</td>
<td></td>
<td></td>
</tr>
<tr>
<td>COPD</td>
<td>82 (19)</td>
<td>22 69</td>
<td>80</td>
<td>94</td>
<td>182</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>58 (14)</td>
<td>15 49</td>
<td>57</td>
<td>67</td>
<td>135</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>23 (7)</td>
<td>4 18</td>
<td>23</td>
<td>28</td>
<td>58</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Air pollution, µg/m$^3$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM$_{10}$</td>
<td>48.6 (27.3)</td>
<td>7.6 27.2</td>
<td>42.9</td>
<td>64.5</td>
<td>572.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NO$_2$</td>
<td>55.6 (19.6)</td>
<td>12.9 41.4</td>
<td>52.7</td>
<td>66.3</td>
<td>167.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>O$_3$</td>
<td>36.3 (21.8)</td>
<td>3.1 19.1</td>
<td>31.3</td>
<td>45.3</td>
<td>134.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relative humidity, %</td>
<td>78.4 (10.2)</td>
<td>29.0 74.0</td>
<td>79.0</td>
<td>85.0</td>
<td>99.0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: SD = standard deviation; Min = minimum; Max = maximum; COPD = chronic obstructive pulmonary disease; PM$_{10}$ = particulate matter with aerodynamic diameter ≤ 10 µm; NO$_2$ = nitrogen dioxide; O$_3$ = ozone.
(Supplemental Table S1). Next, we added a linear interaction term between time (centred on 1st July, the middle day of each corresponding year) and the created cross-basis term of temperature to estimate the year-specific association of temperature with respiratory hospitalizations (Gasparrini et al., 2015a). A detailed description of the time-varying DLNM has been published elsewhere (Gasparrini et al., 2015a; Gasparrini et al., 2016).

We identified optimum temperature by selecting the temperature with the minimum hospitalization risk between 1st and 99th percentile of overall cumulative temperature-hospitalizations association for each cause of respiratory diseases (i.e., total respiratory, pneumonia, and COPD) from the models without the interaction term (Gasparrini et al., 2015b). We then used the identified minimum hospitalization temperature as the reference temperature to re-center the natural cubic B-spline that models the non-linear effects of temperature. We estimated cold and heat hospitalization risks by computing the relative risk (RR) with reference to the optimum temperature. We performed multivariate Wald test on the interaction term to test whether there was a temporal variation in the cumulative temperature-respiratory hospitalization curves (Gasparrini et al., 2015a).

2.3.2. Trends in temperature-related attributable fraction

We calculated attributable fraction (AF) to quantify the temperature-related hospitalization burdens for respiratory diseases. We estimated year-specific temperature-related AF based on time-varying DLNM. We calculated the yearly heat- and cold-AFs by summing up all days of respiratory hospitalizations where temperatures were above or below the identified optimum temperature, we then dividing by the yearly total number of respiratory hospitalizations (Gasparrini and Leone, 2014). We also calculated the year-specific total temperature-AFs for respiratory hospitalizations via dividing the yearly total number of respiratory hospitalizations by the yearly total temperature attributable hospitalizations (Gasparrini and Leone, 2014). We then obtained the empirical confidence intervals (empirical CIs) for AF by Monte Carlo simulations simulating 5000 samples from a multivariate normal distribution of the coefficients (Gasparrini and Leone, 2014). We tested the temporal change in year-specific AF by performing a meta-regression model with year as the predictor and year-specific AF as the dependent variable.

The role of air pollution on the health effects of temperature is complex (Buckley et al., 2014). In the current study, with and without adjusting for air pollution (PM$_{10}$, NO$_2$, and O$_3$) resulted in similar risk estimates for temperature effects. We conducted all analyses in statistical environment R version 3.5.1 with “dlnm” package version 2.3.6 to model the non-linear and delayed effects of temperature and the “attrdl” function to calculate AFs.

3. Results

3.1. Descriptive results

During the study period, a total of 1,639,303 emergency hospital admission for respiratory diseases were recorded. On average, there were 264 emergency hospital admissions for respiratory diseases per day, of which males and females accounted for 59% and 41%, respectively. Pneumonia accounted for over one-third of all respiratory

![Fig. 1. Violin plots of the daily emergency hospital admissions for respiratory diseases (count), ambient temperature (°C) and relative humidity (%) by year in Hong Kong. Abbreviation: COPD = chronic obstructive pulmonary disease; RH = relative humidity. The white vertical central bar indicates the interquartile range and the black horizontal bar indicates the median value. The filled colour of violin plots indicates yearly mean count of hospitalization, ambient temperature or relative humidity. (For interpretation of the references to colour in this figure legend, the reader is referred to the online version of this chapter.)](image-url)
hospitalizations (36%), whereas COPD accounted for 31%. The daily 24-hour mean concentration of air pollution was 48.6 μg/m³ for PM2.5, 55.6 μg/m³ for NO2, and 36.3 μg/m³ for O3, respectively. The average daily mean temperature was 23.5 °C, with a range varying from 4.9 °C to 32.4 °C, and the mean relative humidity was 78.4% (Table 1).

The violin plots show the distribution of emergency respiratory hospitalizations, ambient temperature and relative humidity (Fig. 1). The number of emergency hospital admissions for total respiratory and pneumonia was increasing in recent years, but was general constant for COPD hospitalizations. From 2000 to 2016, the yearly mean ambient temperature was constant in general, but its variation was becoming wider.

3.2. Trends in magnitude of the association

Table 2 shows the trend in magnitude of the association between respiratory hospitalizations and temperature. We used the Wald test on the interaction term between the cross-basis term of temperature and time to test whether there was an overall temporal change in the cumulative temperature-hospitalizations relationship. We found a statistically significant temporal variation for respiratory hospitalization (p for interaction < 0.001) and pneumonia (p for interaction < 0.001), but not for COPD (p for interaction = 0.117). The changing patterns of the cumulative temperature-hospitalizations relationship were similar among sex groups. For example, the temporal variations in the associations for males were statically significant for total respiratory (p for interaction < 0.001) and pneumonia (p for interaction < 0.001), but not for COPD (p for interaction = 0.325). To figure out whether the trend was increasing or decreasing, we graphically evaluated the dose-response curves for the interaction terms to examine how time modified the temperature-respiratory hospitalizations relationship (Fig. 2). We found the associations for cold showed an attenuated trend, but the associations for heat were increasing over the study period for total respiratory and pneumonia (Fig. 2, Supplemental Fig. S2 and Supplemental Fig. S3). For example, RR for moderate cold decreased from 1.59 (95% CI: 1.42, 1.79) in 2000 (the first year of the study period) to 1.12 (95% CI: 1.02, 1.24) in 2016 (the last year of the study period), whereas RR for extreme heat increased from 1.01 (95% CI: 0.93, 1.08) in 2000 to 1.29 (95% CI: 1.19, 1.39) in 2016 for total respiratory diseases.

3.3. Trends in temperature-related attributable fraction

Figs. 3 and 4 show the trend in the temperature-related AF for respiratory diseases and by sex from 2000 to 2016. The p-value for the trend in the year-specific AF was summarized in Supplemental Table S2. We consistently observed a substantial increase in heat-AFs for total respiratory, pneumonia, and COPD. For example, the heat-AFs from 2000 to 2016 increased from 0% (95% empirical CI: −1%, 1%) to 3% (95% empirical CI: 2%, 4%) for total respiratory, from 0% (95% empirical CI: −1%, 2%) to 4% (95% empirical CI: 2%, 5%) for pneumonia, and from 0% (95% empirical CI: −1%, 1%) to 1% (95% empirical CI: 0%, 2%) for COPD. The increasing trend in heat-AFs was similar by sex groups. The temporal changes in cold-AFs differed by causes of respiratory diseases, with roughly no change in AF for total respiratory (p for trend = 0.319), continuous decreasing for pneumonia (p for trend = 0.005), and sharp increasing for COPD (p for trend = 0.001) with AF was 12% and 8% for total respiratory, 15% and 6% for pneumonia, and 10% and 15% for COPD in 2000 and 2016, respectively. The total temperature-related AF (sum of cold- and heat-AF) remained constant over the study period for total respiratory and pneumonia, but substantially increased for COPD. The total-AF for COPD was increasing from 10% (95% empirical CI: 2%, 17%) in 2000 to 17% (95% empirical CI: 11%, 22%) in 2016.

Table 2

<table>
<thead>
<tr>
<th>Disease</th>
<th>Subgroup</th>
<th>OTP</th>
<th>Period</th>
<th>Extreme cold</th>
<th>Moderate cold</th>
<th>Moderate heat</th>
<th>Extreme heat</th>
<th>p for interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory</td>
<td>Total</td>
<td>66th</td>
<td>2000-16</td>
<td>1.64 (1.53, 1.76)</td>
<td>1.32 (1.25, 1.39)</td>
<td>1.06 (1.04, 1.09)</td>
<td>1.14 (1.10, 1.19)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>2000</td>
<td></td>
<td>1.71 (1.47, 2.00)</td>
<td>1.59 (1.42, 1.79)</td>
<td>1.01 (0.96, 1.05)</td>
<td>1.01 (0.93, 1.08)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>2016</td>
<td></td>
<td></td>
<td>1.55 (1.34, 1.79)</td>
<td>1.12 (1.02, 1.24)</td>
<td>1.12 (1.08, 1.17)</td>
<td>1.29 (1.19, 1.39)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>2000</td>
<td></td>
<td>1.65 (1.52, 1.78)</td>
<td>1.33 (1.25, 1.41)</td>
<td>1.07 (1.04, 1.09)</td>
<td>1.15 (1.10, 1.20)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>2016</td>
<td></td>
<td></td>
<td>1.63 (1.56, 1.73)</td>
<td>1.32 (1.25, 1.41)</td>
<td>1.18 (1.05, 1.16)</td>
<td>1.25 (1.14, 1.36)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>Total</td>
<td>62th</td>
<td>2000-16</td>
<td>1.74 (1.57, 1.93)</td>
<td>1.22 (1.22, 1.43)</td>
<td>1.09 (1.06, 1.13)</td>
<td>1.19 (1.12, 1.26)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>2000</td>
<td></td>
<td>1.90 (1.47, 2.46)</td>
<td>1.90 (1.56, 2.32)</td>
<td>1.00 (0.93, 1.09)</td>
<td>0.98 (0.85, 1.11)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>2016</td>
<td></td>
<td></td>
<td>1.63 (1.33, 1.99)</td>
<td>1.04 (0.91, 1.19)</td>
<td>1.16 (1.09, 1.24)</td>
<td>1.36 (1.22, 1.51)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>2000</td>
<td></td>
<td>1.84 (1.62, 2.08)</td>
<td>1.40 (1.27, 1.54)</td>
<td>1.10 (1.05, 1.15)</td>
<td>1.20 (1.12, 1.29)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>2016</td>
<td></td>
<td></td>
<td>2.27 (1.64, 3.13)</td>
<td>2.01 (1.57, 2.59)</td>
<td>1.02 (0.92, 1.12)</td>
<td>1.00 (0.84, 1.18)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>COPD</td>
<td>Total</td>
<td>75th</td>
<td>2000-16</td>
<td>1.79 (1.61, 1.99)</td>
<td>1.43 (1.23, 1.64)</td>
<td>1.03 (1.01, 1.05)</td>
<td>1.08 (1.03, 1.14)</td>
<td>0.117</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>2000</td>
<td></td>
<td>1.64 (1.31, 2.06)</td>
<td>1.35 (1.13, 1.60)</td>
<td>1.01 (0.97, 1.06)</td>
<td>1.04 (0.95, 1.13)</td>
<td>0.002</td>
</tr>
<tr>
<td></td>
<td>2016</td>
<td></td>
<td></td>
<td>2.02 (1.61, 2.54)</td>
<td>1.35 (1.15, 1.58)</td>
<td>1.04 (1.00, 1.10)</td>
<td>1.13 (1.02, 1.25)</td>
<td>0.032</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>2000</td>
<td></td>
<td>1.73 (1.53, 1.95)</td>
<td>1.31 (1.19, 1.45)</td>
<td>1.03 (1.00, 1.06)</td>
<td>1.08 (1.03, 1.15)</td>
<td>0.325</td>
</tr>
<tr>
<td></td>
<td>2016</td>
<td></td>
<td></td>
<td>2.04 (1.11, 1.86)</td>
<td>1.28 (1.05, 1.56)</td>
<td>1.03 (0.98, 1.08)</td>
<td>1.07 (0.97, 1.19)</td>
<td>0.117</td>
</tr>
</tbody>
</table>

Abbreviation: OTP = optimum temperature percentile; COPD = chronic obstructive pulmonary disease; RR = relative risk; CI = confidence interval.

- Estimated as the minimum of the overall cumulative exposure-response curve from the model without interaction term.
- Extreme cold was defined as the 1st percentile of temperature (11.3 °C).
- Moderate cold was defined as the 10th percentile of temperature (16.0 °C).
- Extreme heat was defined as the 99th percentile of temperature (30.6 °C).
- p for interaction indicates whether there was a significant difference among overall temperature-respiratory hospitalization associations during the study period.
Emerging studies examined the temporal variation in the temperature-mortality association and reported inconclusive findings (Chung et al., 2017; de’Donato et al., 2015; Gasparini et al., 2016; Lee et al., 2018b; Sheridan and Allen, 2018; Vicedo-Cabrera et al., 2018). By summarizing a total of 70 articles that examined the trend in heat-related mortality, a recent literature review concluded that the heat-mortality association was generally showing a decreasing trend (Sheridan and Allen, 2018). A multi-country study conducted in 305 locations from ten countries (including Australia, Ireland, Brazil, Canada, Japan, South Korea, USA, Spain, Switzerland, and UK) found that most countries showed a similar reduction trend in heat-mortality association, although some did not reach statistically significant, except Australia where the trend of the association was increasing (Vicedo-Cabrera et al., 2018). A nine-cities-based European study also found a significant reduction in the susceptibility to heat in most cities, but observed an increased susceptibility in Helsinki and Stockholm (de’Donato et al., 2015).

Most prior studies investigated the trend in heat-mortality association but only a few evaluated the changes in cold-related mortality. Among those few studies that examined how the population responded to cold temperature over time, findings were not consistent (Lee et al., 2018b; Vicedo-Cabrera et al., 2018). For example, the multi-country study from ten countries found the cold-mortality association showed heterogeneous trends, decreasing for Australia, Ireland, Switzerland, and Spain, increasing for South Korea, or stable for the other countries (Vicedo-Cabrera et al., 2018).

To our best knowledge, our study was the first to examine the temporal trends in the temperature-respiratory hospitalizations association. We found an increasing trend for the magnitude of associations between heat and emergency hospital admissions for total respiratory, pneumonia, and COPD, suggesting an increased susceptibility to heat, which was consistent with several prior studies (Akihiko et al., 2014; Li et al., 2017), but not with others that reported a decreased mortality susceptibility to heat (de’Donato et al., 2015; Sheridan and Allen, 2018). Our findings were in line with an earlier long-term ambient temperature study in Hong Kong which demonstrated an increasing trend of summer discomfort over the past four decades from 1968 to 2008 in Hong Kong (Lam et al., 2010). The climate of Hong Kong is subtropical, and the summer is hot and humid. Due to the extensive use of air conditioning, heat effects are usually not evident (Qiu et al., 2016; Sun et al., 2016; Yi and Chan, 2015). Our findings highlight that attention should be paid to extremely high temperatures in Hong Kong in the future, especially in the context of climate change. The underlying reason for this increased susceptibility to heat is not clear. We did stratified analysis by age groups (<65 years and ≥65 years), and found that the increased susceptibility to heat was more obvious for patients aged <65 years (Fig. S4). Further studies are needed to identify the underlying reasons for the observed temporal changes.

The susceptibility to cold for total respiratory and pneumonia emergency hospitalizations demonstrated a reduction trend. The apparently increasing trend for COPD was not statistically significant. Our findings were generally in line with temporal variation in cold-mortality associations in the UK, Australia, Switzerland, Ireland, and Spain in the multi-country study (Vicedo-Cabrera et al., 2018). The exact reason why we

---

**Fig. 2.** Effect modification of time on the overall cumulative temperature–hospitalization relationships for respiratory diseases. Abbreviation: COPD = chronic obstructive pulmonary disease. Plots show the dose-response curves for the interaction terms between time and the cross-basis term of temperature. The two vertical dashed lines from left to right represent extreme cold (1st percentile of temperature) and extreme heat (99th percentile), respectively. Red solid lines indicate heat (temperatures above the optimum temperature). The grey shaded areas represent 95% confidence intervals. The relative risk and its corresponding 95% confidence interval below or above 1 indicate a significant decreasing or increasing trend for temperature-related risks. For example, the relative risk of extreme heat for total respiratory above 1 means the relative risk for extreme heat from 2000 to 2016 showing a significant increasing trend. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)
found heterogeneous trends for cold-hospitalization association for total respiratory, pneumonia and COPD is unknown. The possible reasons might include changes in housing infrastructure, healthcare services, and the general awareness of cold. However, potential mechanisms to drive the temporal variation in cold-related risk and burden were complex (Ebi and Mills, 2013; Kalkstein and Greene, 1997). Prior studies (Ebi and Mills, 2013; Kalkstein and Greene, 1997) suggested factors not directly related to cold temperature such as seasonal variation of immune system function, diet habit, and other behaviour changes, might play a role.
To quantify the impact of temperature on respiratory hospitalizations, we calculated temperature-related AF, which takes into account both of the magnitude of the association (RR) and distribution of temperature (Gasparrini and Leone, 2014). The temperature-AFs could complement temperature-related risk (RR) to understand the impact of temperature. Few studies have examined the trends of temperature-related AFs, and most of them focused on mortality (Lee et al., 2018b; Vicedo-Cabrera et al., 2018). We found total temperature-related AFs for respiratory hospitalizations remained unchanged during the past 17 years with increasing trends for heat-AFs whereas decreasing trends for cold-AFs. Given that climate change is expected to increase the mean temperature and change the distribution of temperature, the overall respiratory hospitalization burden associated with non-optimum temperatures is not likely to decrease or may be even increasing, which may inform public health policies in the context of climate change.

This study has some limitations. We used one representative fixed-site weather monitoring station located in the urban areas to represent the whole population ambient temperature exposure rather than individual direct measurements, which may result in exposure measurement errors. Also, as our study period is across 17 years during which period the progressive urbanization of Hong Kong would have increased ambient temperature by urban heat island effects. However, we adopted a time-series study which compared day to day variation in ambient temperature and day to day variation in respiratory hospital admissions, so the long-term trend in ambient temperature changes would not introduce bias into the temperature effects assessment. To our best knowledge, this is the first study to comprehensively assess the temporal variations in the association between ambient temperature and respiratory hospitalizations and the temperature related attributable risks. Findings of this study should enrich our understanding of the impact of temperature and shed light on how climate change will influence respiratory hospital admissions in Hong Kong. Our findings could also inform current public health policy and respiratory health professionals.

5. Conclusion

In conclusion, we found a reduction in respiratory hospitalizations susceptibility to cold but an increased susceptibility to heat in Hong Kong. The overall hospitalization burden attributable to non-optimum temperatures was generally stable for respiratory diseases over the past two decades in a subtopic city. Non-optimum temperature is still a significant risk factor for respiratory hospital admissions, especially in the context of climate change.

Acknowledgments
We thank the Hospital Authority for providing the emergency hospital admissions data, the Hong Kong Environmental Protection Department for the air pollution data, and the Hong Kong Observatory for the temperature and relative humidity data.

Conflict of interest
None.

Source of support
None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2019.02.229.

References


