



# The association between short and long-term exposure to PM<sub>2.5</sub> and temperature and hospital admissions in New England and the synergistic effect of the short-term exposures

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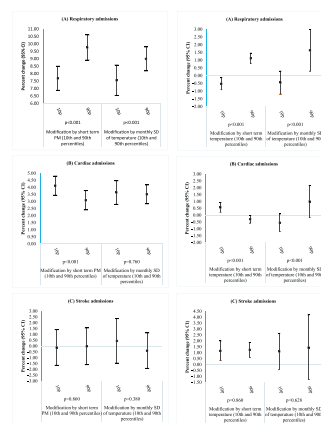
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## HIGHLIGHTS

- Associations between short and long-term exposures were observed for all outcomes.
- Long-term exposures to particulate matter < 2.5 μm (PM<sub>2.5</sub>) had stronger effects than short-term exposures.
- Short-term PM<sub>2.5</sub> related respiratory risk was larger on warmer days.
- Short-term PM<sub>2.5</sub> related cardiac risk was larger on colder days.
- Short-term PM<sub>2.5</sub> risks were larger in months of higher temperature variability.

## GRAPHICAL ABSTRACT



## ARTICLE INFO

### Article history:

Received 13 January 2018

Received in revised form 25 April 2018

Accepted 15 May 2018

Available online xxxx

Editor: Lidia Morawska

### Keywords:

Particulate matter  
Temperature  
Hospitalizations  
Respiratory  
Cardiac

## ABSTRACT

**Background:** Particulate matter < 2.5 μm in diameter (PM<sub>2.5</sub>) and heat are strong predictors of morbidity, yet few studies have examined the effects of long-term exposures on non-fatal events, or assessed the short and long-term effect on health simultaneously.

**Objective:** We jointly investigated the association of short and long-term exposures to PM<sub>2.5</sub> and temperature with hospital admissions, and explored the modification of the associations with the short-term exposures by one another and by temperature variability.

**Methods:** Daily ZIP code counts of respiratory, cardiac and stroke admissions of adults ≥65 (N = 2,015,660) were constructed across New-England (2001–2011). Daily PM<sub>2.5</sub> and temperature exposure estimates were obtained from satellite-based spatio-temporally resolved models. For each admission cause, a Poisson regression was fit on short and long-term exposures, with a random intercept for ZIP code. Modifications of the short-term effects were tested by adding interaction terms with temperature, PM<sub>2.5</sub> and temperature variability.

**Results:** Associations between short and long-term exposures were observed for all of the outcomes, with stronger effects of long-term exposures to PM<sub>2.5</sub>. For respiratory admissions, the short-term PM<sub>2.5</sub> effect (percent increase per IQR) was larger on warmer days (1.12% versus −0.53%) and in months of higher temperature variability (1.63% versus −0.45%). The short-term temperature effect was higher in months of higher

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temperature variability as well. For cardiac admissions, the PM<sub>2.5</sub> effect was larger on colder days (0.56% versus −0.30%) and in months of higher temperature variability (0.99% versus −0.56%).

**Conclusions:** We observed synergistic effects of short-term exposures to PM<sub>2.5</sub>, temperature and temperature variability. Long-term exposures to PM<sub>2.5</sub> were associated with larger effects compared to short-term exposures.

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## 1. Introduction

Particulate matter air pollution and heat are strong predictors of cardiovascular (Yitshak-Sade et al., 2015; Kloog et al., 2012; Kloog et al., 2015; Brook et al., 2010; Barnett et al., 2006; Peters et al., 2001; Ye et al., 2012; Michelozzi et al., 2009; Schwartz et al., 2004) and respiratory (Kloog et al., 2012; Michelozzi et al., 2009; Bell et al., 2008; Kloog et al., 2014a) morbidity and mortality. It is, therefore, important to correctly identify their joint effect on health outcomes, especially in light of the ongoing process of climate change (McMichael et al., 2006; Li et al., 2017). In most studies that assessed the effects of temperature and particulate matter smaller than 2.5 µm in diameter (PM<sub>2.5</sub>) on health, temperature was treated as a confounder rather than a modifier (Li et al., 2017). Those that did assess modification by temperature mostly focused on the estimation of short-term PM effects with stratification by temperature or season. Very little evidence is currently available on synergism (that is, on the joint effects of temperature, temperature variability and air pollution) (Zanobetti and Peters, 2015). In addition, examination of the health effects of temperature has been almost exclusively focused on short-term exposures (days to a few weeks). However, recent studies of mortality cohorts have indicated that there are chronic effects of longer-term temperature exposure, and that temperature variability is a key predictor of health (Shi et al., 2016a; Shi et al., 2015; Anderson and Bell, 2009; Breitner et al., 2014; Guo et al., 2016). Such exposures have not, to our knowledge, been studied for hospital admissions for acute events.

The underlying mechanism explaining the interaction between temperature and PM may be related to different exposure patterns to PM across the range of temperature (i.e. different PM composition in warmer and colder temperatures) (Stafoggia et al., 2008) or to physiological stress that may increase susceptibility (Li et al., 2015a). Regarding temperature variability, there is strong evidence of adaptation to usual temperatures (Zanobetti et al., 2012), and because the effect of climate change is seen both in the increases of the average values and the variability of temperature (Stocker, 2014), it is important to investigate the health impacts of unstable weather and its interaction with PM.

The majority of studies that examined the interaction between temperature and PM focused on mortality (Li et al., 2017; Breitner et al., 2014; Stafoggia et al., 2008; Li et al., 2015a; Kioumourtzoglou et al., 2016; Sun et al., 2015; Li et al., 2015b; Analitis et al., 2014; Burkart et al., 2013; Kim et al., 2015a; Dholakia et al., 2014; O'Neill et al., 2003; Shi et al., 2016b; Wang et al., 2017). The evidence regarding hospital admissions, emergency room visits or other measures of morbidity are scarce, and the direction of the interaction varies by the outcome tested and the geographic location. A study by Pan et al. assessed the modification of the association between temperature and measures of cerebrovascular hemodynamics, by PM<sub>2.5</sub>. The authors found significantly weaker effects of temperature on resting blood flow velocity at higher PM<sub>2.5</sub> concentrations (Pan et al., 2015). A recent study has found an increased risk of stroke associated with PM<sub>2.5</sub> on the day of the event, with stronger associations on warmer days (Huang et al., 2016). A study in New York, which included hospital admissions due to cardiovascular diseases, found stronger associations with PM<sub>2.5</sub> in the winter and in low temperatures (Hsu et al., 2017). For respiratory admissions, a study of 204 US urban counties found stronger effects of

PM<sub>2.5</sub> in warmer regions (Dominici et al., 2006). Another study, however, found stronger short-term PM<sub>2.5</sub> effects in the winter (Bell et al., 2008).

Another gap is that most previous research examined either acute or chronic exposure rather than investigating the effect of both exposures simultaneously (Zanobetti and Peters, 2015). Examining the simultaneous effect of both exposures will provide the effect of each exposure independently from the other. Kloog and colleagues addressed this in a series of studies, where they investigated both acute and chronic effect of air pollution on several health outcomes and found increases of short and long-term exposure to PM<sub>2.5</sub> to be associated with increases in cardiovascular, respiratory and stroke admissions rate (Kloog et al., 2012; Shi et al., 2016b; Kloog et al., 2013), but further examination of the potential interactions of these effects is clearly needed.

In this study, we aim to investigate the association between short and long-term exposures to PM<sub>2.5</sub> and temperature simultaneously, with cardiac, stroke and respiratory hospital admissions, while using spatio-temporally resolved satellite based exposure models (Kloog et al., 2014b; Kloog et al., 2014c). In addition, we aim to explore the modification of the associations with the short-term exposures by one another and by temperature variability, which may limit physiological adaptation to temperature.

## 2. Methods

### 2.1. Study population and main outcomes

This study was approved by the Harvard School of Public Health Institutional Review Board. The study population comprised New England residents between the years 2000 and 2011, 65 years or older, who were Medicare beneficiaries and enrolled in the fee-for-service program. For each eligible subject, individual-level data on gender, age, race, country of residence, Medicaid eligibility, dates of hospital admissions, the International Classification and Disease, Ninth Revision (ICD 9) code for the primary cause of hospitalization and the date of death were extracted. Cases were defined as emergency admissions with a principal discharge code of all respiratory diseases (ICD 9: 460–519), all cardiac diseases (ICD 9: 390–429) or ischemic stroke (ICD 9: 432–435). From this data, we constructed daily counts of the number of hospital admissions for each admission cause and each zip code.

### 2.2. Exposure

Temperature data were obtained from a spatiotemporally resolved prediction model generating predictions of daily average temperatures at a 1 × 1 KM spatial resolution, described previously in detail (Kloog et al., 2014c). In brief, daily MODIS (Moderate resolution imaging spectroradiometer) land surface temperatures (LST) data, in grid cells where both air temperature and LST were available for that day, were calibrated using mixed effect models. The model covariates included LST, land use regression (LUR) variables (percent urban, elevation, normalized difference vegetation index) and a random intercept and slope for surface temperature for each day. Information from neighboring grid cells was used to estimate air temperature when no surface temperature data are available. Out-of-sample ten-fold cross-validation was used to quantify the accuracy of the model predictions, showing

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