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## Disentangling interactions between atmospheric pollution and weather

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### Abstract

The association between short-term exposure to extreme weather events and health has been well established. In addition, there is a large body of epidemiological literature on the short and long-term effects of ambient exposure to PM<sub>2.5</sub>.

We hypothesize that the health impact associated with exposure to air pollution and weather is larger than the risk estimated based on the health effects of air pollution and weather alone. Not much work has been done to estimate the acute and chronic effects associated with simultaneous exposure to multiple environmental agents such as weather and particulate matter.

In this editorial we highlight challenges in addressing these interactions. Around the globe, exposure to weather parameters, composition of gaseous and particulate air pollution, and the ventilation rates vary by season. Furthermore, weather and pollution mixtures exhibit different exposure-response function and act through different pathophysiological mechanisms. The synergistic analysis of ambient air pollution and weather require studies collecting appropriate data and advancing methodological approaches. Due to large variation in space and time, carefully designed multi-center studies will be important to address these challenges and provide novel stimuli for promoting measures to slow climate change and improve air pollution in urban areas and in cities around the world.

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### The impact of climate change

The new Intergovernmental Panel on Climate Change (IPCC) report re-affirm the mounting threat of climate change[1]. The IPCC predicts that global average surface temperature will increase by 1.4 to 5.8 degrees Celsius by the end of this century, depending on pollution emissions scenarios and the sensitivity of climate to greenhouse gas perturbations[1].

Climate change perturbs not just surface temperatures, but also a suite of other meteorological variables important to human health, including absolute humidity, surface pressure, precipitation, and the duration and intensity of summertime weather. Forecasting studies suggest that in the Northeast United States, the passage of summertime cold fronts

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will diminish in frequency in a warmer climate, leading to more persistent heat waves. Observations show that such a trend in cold front frequency in the Northeast may have already begun. In a warming climate, absolute humidity will likely increase due to increased surface evaporation [2]. Polluting emissions not only increase climate change, but for example in the Northeast heat waves are usually accompanied by, and can lead to increased secondary pollutants like ozone[3]. On the other hand the impacts of climate change mitigation activities related to energy production, such as the increased use of wind, wave, solar, and nuclear sources of power generation, but also reduction in greenhouse gas emissions are likely to reduce particulate and other air pollution emissions.

## Epidemiological evidence from studies on weather and air pollution

Increased mortality has been linked, not only to heat wave episodes[4], but also to exposure to colder weather conditions [4–7]. In general, morbidity[8,9] and mortality[10,11] associated with heat depends on age, race, sex, class, home characteristics, access to air conditioning, general health and living in an urban area versus a rural area[12]. Greater susceptibility to extreme heat has been reported for: the elderly; children; impoverished populations/those with lower socioeconomic status; pregnant women; people with chronic health conditions (e.g., diabetes, mobility and cognitive constraints); and outdoor workers [8,11,13–16]. Panel studies investigating associations between temperature and cardiac risk factors such as increased blood pressure[17–19], markers of inflammations[15,20–22], and cholesterol[23,24], or changes in heart rate and repolarization parameters[25], have shown divergent results, suggesting that mechanisms for weather-related cardiovascular deaths are still to be elucidated. Inconsistent results in small observational studies with potentially susceptible individuals can have multiple sources including differences in panel composition and therefore underlying susceptibility as well as differences in exposure ranges depending on the season. The later point may be of great importance as potentially pathomechanisms of cold and hot weather responsible for associations with mortality and morbidity may differ. Cold temperatures may induce pro-inflammatory and pro-coagulatory states, while in contrast, evidence from patients with heat stress or heat strokes indicates anti-coagulatory states to promote sweating and decrease body temperatures.

Temperature is not the only weather exposure. Barometric pressure has been used as a covariate in several previous studies[14,26], however, studies focusing on exposures to air pollution have often abstained from adjusting for it due to the fact that low pressure periods in winter time are the reason for elevated air pollution concentrations from local sources. The only two that examined the independent barometric pressure health effects found protective associations with mortality[26] and pulse rate[27]. Precipitation, in the form of snowfall has been mainly related to shovel-related injuries and exercise induced medical emergencies. In contrast, rainfall in moderate amounts may improve health by reducing ambient air pollution and pollen levels. Water vapor pressure, a measure of humidity has been associated with ST-segment [9] and brachial artery diameter[28]. High humidity has been associated with hyperpyrexia, decline in physical strength and fatigue; reduction in alertness and mental capacity, but it often occurs when temperature is high.

It is highly likely that temperature does not act alone in determining health, but rather in concert with other weather parameters, ambient air pollutants and aerosols of biological origin. For example, allergen patterns are also changing in response to climate change, and air pollution can modify the allergenic potential of pollens. However joint effects of multiple weather parameters and air pollutants on health have not been well-explored. There are some studies indicating synergism between temperature and air pollution[3,29–33], showing higher pollution effects with hotter weather, and also that the effects of temperature can be overstated if one fails to control for air pollution[34]. A recent review [35] showed that the methods used to assess the synergism between temperature and air pollution have been mainly focused on the estimation of air pollution health effects stratified by season or by interaction. Therefore, development of studies optimizing the collection of appropriate data and advancing methodological approaches to better assess the complex interplay between weather and ambient aerosols are needed.

## Moving forward

We hypothesize that the health impact associated with exposure to air pollution and weather jointly is larger than the risk estimated based on the health effects of air pollution and weather alone. The comprehensive assessment of short-term variation of air pollution and weather on health seems to be highly challenging, but the joint impact on a regional scale and over longer time periods has not been explored yet. Specifically, we hypothesize that weather variability together with elevated long-term exposures to ambient air pollution is contributing to the burden of chronic diseases. Addressing these hypotheses poses a number of challenges which we would like to examine more closely in the following sections.

## Varying exposure contrasts around the world

Ambient air pollution mixtures differ between seasons and region (table 1). Not only does the composition of fine particulate matter (PM<sub>2.5</sub>, particulate matter smaller than 2.5 μm in aerodynamic diameter), the single pollutant with the largest health impact, differ, but also the co-occurring gaseous pollutants differ. In addition, exposure ranges differ by season when comparing the evidence on a global scale.

The highest PM<sub>2.5</sub> concentrations are observed during the summer months in Northern America, being dominated by regional transported secondary aerosols for which sulfates are a marker. In contrast, the highest concentrations of PM<sub>2.5</sub> are reported during the winter months in Europe resulting from a combination of local sources and regional transport for which black carbon can be considered a marker. Behavioral changes modify population average exposures as well. During cold seasons, air exchange rates decrease and therefore decreasing exposures to air pollution from outdoor origin as well. In the presence of widespread air condition use, the exposure to air pollution is reduced in the summer months while increasing energy consumption. Obviously, outside the tropics, temperatures differ by season as well. Generally, perceived temperatures differ by accompanying weather conditions such as humidity or wind chill. These modifying conditions are summarized in measures such as apparent temperature.

### Short-term exposure-response function

A substantial additional challenge which becomes important when studying interactions is the fact that the exposure-response functions differ greatly when considering ambient air pollution and temperatures. The associations between ambient air pollution and health outcomes are considered to be linear in the low to medium exposure range with a potential flattening of the function at very high concentrations[36]. In contrast, associations between temperature and health outcomes are reported to be u- or j-shaped with some variation across different climate zones[7]. Interestingly, the optimal temperature range seemed to vary by climate zones. In Figure 1 we show our hypothesis that the combination of temperature and air pollution increases mortality both in winter and in summer/spring. As summarized in table 1, the impact of temperature and air pollution in winter originates from cold and local pollution. In summer, heat and secondary pollution on a regional (PM) and local scale (ozone) are responsible for the increased risk. In polluted climates and hot climates, we hypothesize that the risk is larger than the sum of the individual risks (figure 1, brown line).

### Short-term effect's lag structure and susceptibility

Studies assessing the short-term health effects of environmental exposures explored different lag-structures and found evidence that air pollutants may have very immediate effects on some specific disease outcomes such as myocardial infarctions, while other disease outcomes such as chronic obstructive disease mortality may have stronger associations with cumulative exposures over several days. Similarly, immediate and cumulative responses to temperature changes were observed and the lag structures were documented to differ between cold and hot periods. Therefore models to assess interactions with different lag structures are needed.

### Study the interactions of long-term exposures

Mounting evidence suggests that long-term exposure to air pollution has major health impacts; nevertheless the long-term effect of weather changes due to weather is nearly unexplored. A study was performed by Zanobetti and colleague[37], who assessed the impact of temperature variability on mortality in a prospective analysis of Medicare data. They found that particularly among elderly (age larger than 74 years) and chronically ill individuals, variability in temperature was consistently associated with mortality. No investigations have assessed the associations between long-term exposures to temperature and air pollution jointly. An assessment of the joint effects of long term exposure of air pollution and weather is difficult because the exposure response functions on the margins are not well developed and investigated. The same is true for an assessment of the relevant time window of exposure.

### Integrating designs and methods for short and long term studies

Integrated concepts to assess health effects of short and long-term exposures seems to be the way forward to revolutionize the assessment of weather and urban ambient air jointly. Innovative study designs and methods are needed. Specifically, there is the need to evaluate both short and long term temperature pollution interactions, and the disease development

due to temperature-pollution interactions in large cohorts with well characterized populations in different areas of the world. This would permit to study how the synergistic effect may vary among cities according to local weather characteristics, activity patterns and physical adaptation. A focus on large cohorts would allow in addition to study susceptible individuals with pre-existing diseases to evaluate short and long term effects.

Ideally, newly emerging methods should be systematically applied to large scale cohorts, capturing the health effects of weather variability and pollution mixture, together with their interaction around the world. Statistical methods addressing the challenges described above are under way, especially using spline methodologies for interactions; integrating the exposure-response functions with distributed lag models; and applying Bayesian hierarchical model addressing short and long term exposure jointly; as well as others.

## Outlook

In conclusion, the combined analysis of ambient air pollution and weather jointly poses more challenges than currently acknowledged by most attempts to tackle them. However, due to large variation in space and time, carefully designed multi-center studies are considered potent to meet the challenges at hand. Leveraging the variation in exposures also on a global scale would allow capturing the interactions between weather and ambient air pollution jointly to a full extend. In addition, these studies will provide novel stimuli for promoting measures to slow climate change and improve air pollution in urban areas and in particular in megacities around the world.

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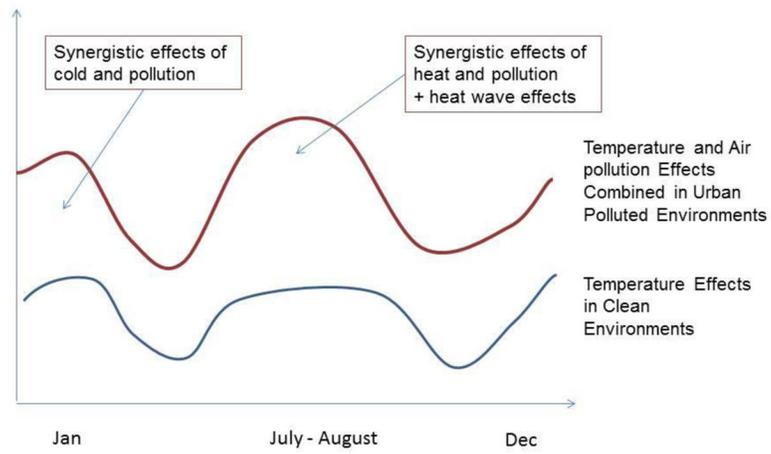
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**Figure 1.** Hypothetical relationship between mortality and the combination of temperature and air pollution by season.

**Table 1**

Schematic descriptions of differences in environmental conditions between seasons in temperate climates of the Northern hemisphere.

	<b>Winter</b>	<b>Spring</b>	<b>Summer</b>	<b>Fall</b>
North America temperate regions	Low temperatures, cold spells Particles of local and regional origin Moderate NO <sub>2</sub>	Unusually cold or hot days Intermediate pollution Pollen	High temperature, heat waves High particles of regional origin Wildfires High ozone	Unusually cold or hot days Intermediate pollution
Europe temperate regions	Low temperatures High particles of local and regional origin High NO <sub>2</sub>	Unusually cold or hot days Intermediate pollution Pollen	High temperature, heat waves High ozone	Unusually cold or hot days Intermediate pollution
Asia temperate regions	Low temperatures High particles of local and regional origin High NO <sub>2</sub> High SO <sub>2</sub>	Unusually cold or hot days Intermediate pollution Pollen Wildfires Dust storms	High temperature Moderate ozone	Unusually cold or hot days Intermediate pollution