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Climate change, extreme weather events, air pollution and respiratory health in Europe

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Abstract

Due to climate change and other factors, air pollution patterns are changing in several urbanized areas of the world, with a significant effect on respiratory health both independently and synergistically with weather conditions; climate scenarios show Europe as one of the most vulnerable regions. European studies on heat wave episodes have consistently shown a synergistic effect of air pollution and high temperatures, while the potential weather-air pollution interaction during wildfires and dust storms is unknown. Allergens patterns are also changing in response to climate change and air pollution can modify the allergenic potential of pollens especially in presence of specific weather conditions. The underlying mechanisms of all these interactions are not well known; the health consequences vary from decreases in lung function to allergic diseases, new onset of diseases, exacerbation of chronic respiratory diseases, and premature death. These multidimensional climate-pollution-allergen effects need to be taken into account in estimating both climate and air pollution-related respiratory effects in order to set up adequate policy and public health actions to face both the current and future climate and pollution challenges.

Keywords: air pollution; allergens; climate change; extreme weather events; respiratory diseases; susceptibility
Introduction

The continuous increment in anthropogenic emissions of carbon dioxide (CO₂) and other greenhouse gases following the Industrial Revolution is dramatically changing the climate overall and at regional level. As other parts of the world, Europe has experienced a progressive warming (+0.90°C for 1901 to 2005) and an increase in mean precipitation except in some regions (i.e. the Mediterranean Region) that are becoming arid [1, 2]. Climate scenarios for the next century predict that the warming will be associated with more frequent, more intense and longer lasting heat waves especially in Southern and Eastern Europe but also in areas not currently susceptible to such events [2, 3]. This will be paralleled by an increase in the intensity of short duration precipitation events (1 to 2 days) in regions such as the Mediterranean where also a decrease in mean precipitation is expected [2]. The higher intensity of rainfall events will increase the likelihood of floods, especially flash floods, throughout Europe, while the occurrence of heatwaves and droughts will increase the risk of wildfires and desertification notably around the Mediterranean basin [2].

In urban areas, climate change is likely to influence outdoor air pollution levels because the generation and dispersion of air pollutants, such as ozone and particulate matter, depend in part on local patterns of temperature, wind, solar radiation and precipitation [4]. In some regions, air quality is projected to further worsen due to the increased frequency of wildfires that cause the release into the atmosphere of gaseous and particulate pollutants. In addition, changes in wind patterns and desertification will modify the long-range transport of pollutants emitted by human activities and biomass burning [4].

Changing patterns of disease are occurring in response to changing environmental conditions. As widely recognized, air pollution has a significant impact on human health, with a great burden on respiratory diseases, particularly on asthma, rhinosinusitis, chronic obstructive pulmonary disease (COPD) and respiratory tract infections [5]. Changes in climate are expected to additionally aggravate the effect of air pollution on these diseases. Prompted by these scenarios, the American Thoracic Society and the European Respiratory Society have recently expressed their concern on the threat posed by air pollution and climate change on respiratory disease [6, 7]. Current and future impacts on respiratory mortality and morbidity deriving from
changes in climate as well as from trends in air pollutants are therefore a priority for the researchers, respiratory clinicians and policy-makers agenda.

This review summarizes the scientific evidence on the effects of climate-related hazards on respiratory health from epidemiological studies. Specifically, we considered those climate events which may be influenced most by climate change and for which climate conditions are interlinked with air quality: temperature extremes, wildfires and dust storms. The conceptual framework for these interactions is summarized in Figure 1. Pathogenetic mechanisms, vulnerable population subgroups and policy implications are discussed and research needs are identified.

**Climate change and air quality**

Climate change and air pollution are intrinsically connected since greenhouse gases and air pollutants originate from the same source, fossil fuel combustion [8-10]. Combustion processes in fact emit both greenhouse gases, like carbon dioxide, methane (CH\textsubscript{4}) and nitrous oxide (N\textsubscript{2}O), and air pollutants like particulate matter (PM), sulphur dioxide (SO\textsubscript{2}), nitrogen dioxide (NO\textsubscript{2}) and carbon monoxide (CO).

From both a global and a regional level, now and in the future climate change and air pollution trends counterbalance in determining air quality: on the one hand, a reduction in anthropogenic emissions resulting from the implementation of the already adopted emission control legislation in each country and energetic sector improvements, on the other hand climate change effects in most cases leading to an increase in pollution levels [11].

The correlation between climate and air quality is noteworthy for ozone. Ozone levels are directly driven by weather since ozone-generating photochemical reactions of air pollutants (nitrogen oxides, NO\textsubscript{x}; methane; volatile organic compounds, VOCs) need high temperatures and bright sunshine, conditions typical of summer months [11]. High temperatures are often associated with dry weather conditions which significantly contribute to high ozone levels during heat waves through a drought stress on vegetation that inhibits stomatal uptake of ozone [8, 12]. Anthropogenic emissions of ozone precursors will decline in industrialized countries but not in the emerging economies; hemispheric background ozone concentrations will increase due to higher frequency in forest fires [11]. Considering climate change scenarios, a large climate
change-related ozone increase is expected in Southern European regions that will overcome the beneficial reduction in ozone precursor anthropogenic emissions in these countries [11].

Climatic factors affect particulate matter concentrations to a different extent depending on the PM chemical components [8]. On the one hand high temperature results in an increase in sulfate aerosols due to faster \( \text{SO}_2 \) oxidation, and on the other, it brings a reduction in nitrate PM concentrations due to increased gas phase transition [8]. However, under climate change the nitrate burden is predicted to increase as well as all the other aerosol species except sulphates [13]. Over Europe, the predicted increase in overall aerosols concentrations will be by 20–40 µg/m\(^3\), relative to the present-day values [13]. Changes will be driven by precipitation changes since wet deposition represents the primary PM sink but also by increments in water vapor that increase oxidation of \( \text{SO}_2 \) and sulfate concentrations. Another important factor is represented by air stagnation conditions that will increase PM concentrations in polluted regions [4, 8]. Climate change-related increase in wildfires will also influence particulates levels [14, 15]; an increase in fire risk in Mediterranean countries is expected especially in areas with high forest cover [4, 16]. The 2003 heat wave in Europe is emblematic since it was associated with both record wildfires and high PM levels [8]. During wildfires the main concern is on fine particles (particles with diameter lower than 2.5 µm, PM2.5) since they have a longer lifetime (on the order of days) and may be carried for long distances from their source regions [17]. Future PM concentrations are also driven by long-range transport of dust aerosols. The long-range transport of pollutants emitted by human activities, burning biomass and dust will also be influenced by future climate changes due to changes in wind patterns and desertification [4].

Another important linkage between climate and air quality is that primary products of combustion processes (i.e. carbon monoxide, non-methane volatile organic compounds, nitrogen oxides, sulphur dioxide, black carbon, organic carbon aerosol) and some secondary pollutants (i.e. ozone) have the potential to increase global warming directly or indirectly [18]. Carbon monoxide, non-methane VOCs and nitrogen oxides cause a reduction in the oxidant power of the atmosphere increasing the lifetime of methane, one of the most important warming agents and a precursor to ozone [18]. Nitrate particles as well as organic carbon aerosol have instead a
cooling effect on the climate. Sulphur dioxide partly converts to sulphate particles which also have a cooling potential and partly reacts with black carbon which has a strong warming effect [18]. Also wildfires may directly contribute to global warming since they emit large quantities of greenhouse gases (i.e. CO, carbon dioxide, methane) [19].

**Respiratory health effects**

Since the 1990s, an extensive European collaboration has been set up through the EU-funded research programmes in the field of air pollution (APHEA, APHEIS, AIRNET, APHEKOM) and climate change (cCASHh, PHEWE, EuroHEAT, CIRCE) [20]. These studies have substantially contributed to the current epidemiological knowledge on the short-term health effects of air pollution and high temperatures/heat waves in Europe and to the formulation of the WHO guidelines [21] and EU air pollution standards. Several of these projects also specifically investigated the synergy between air pollution and high temperature exposure and heat wave events (PHEWE, EuroHEAT, CIRCE) [22]. The ongoing EU project PHASE (Public Health Adaptation Strategies to Extreme weather events) will provide further insights into the synergy between air pollution and extreme weather events (e.g. heat waves, cold spells) and an innovative aspect will be to investigate also their environmental consequences (floods, wildfires) that are projected to increase with predicted climate change.

**Air pollution effects.**

Respiratory diseases are on the rise worldwide, especially allergic diseases such as asthma and rhinitis [23, 24]. This trend has been documented both in industrialized and developing countries but was greater in regions where prevalence was previously low [23, 24]. However, geographical differences have emerged from studies comparing areas at different urbanization level or Eastern and Western European countries, providing evidence of higher frequency of respiratory allergic diseases in westernised and more urbanised areas [25, 26]. The causes of such large heterogeneity both on the temporal and geographical scales should be searched in environmental exposures since genetic factors cannot change so rapidly to such an extent; outdoor air pollution is one possible explanation of the observed trends [27]. Primary (i.e. oxides of nitrogen, VOC) and secondary pollutants (i.e. ozone) have been associated with a wide range of respiratory health effects, including exacerbations of
diseases in subjects already affected by chronic respiratory illnesses such as asthma and COPD, that account for repeated hospitalizations and emergency department visits for the underlying disease, declines in lung function, asthma attacks, emergency room visits, hospital admissions, premature mortality and, possibly, the occurrence of new respiratory problems, i.e. new-onset asthma [5, 6, 21, 28, 29]. Despite the decreasing current trends in anthropogenic air pollution levels in the US and Europe (although not uniformly) [30], there is strong evidence that air pollutants have an effect on respiratory health even at the low levels actually measured [28]. In Europe since the '90s, the APHEA multicentre project identified and quantified the short-term health effects of these air pollution levels (see Table in online depository). Immediate effects on mortality (lag 0-1) associated with 10 μg/m$^3$ increase in pollutant were 0.4% for NO$_2$ [31], 0.6% for PM10 [32], 0.8% for black smoke and 1.1% for ozone [33]. The delayed effects are even greater, 4.2% for PM10 (lag 0-40) [34], and 3.4% for ozone (lag 0-20) [35]; these pollutants had the most prolonged lagged effects on respiratory mortality compared to total or cardiovascular mortality [34, 35]. Air pollutants have also an effect on hospital admissions for specific causes i.e. PM10 and sulphur dioxide is associated with 0.5-1.5% increase in admissions for asthma and COPD in specific age groups [36-38].

**Outdoor temperature effects.**

European projects have documented that respiratory health is largely affected not only by air pollution but also by weather conditions, especially in 75+ yrs population (Table 1). During summer, each degree increase in maximum apparent temperature (a combined indicator of temperature and humidity) above a city specific threshold level (ranging from 23 to 29°C) is related to circa 7% increase in daily respiratory deaths [39]. A smaller but still significant effect has been observed on respiratory hospital admissions, around 3-5% [40]. The effect of extreme events, i.e. heat waves, is much larger accounting for an increase in respiratory mortality during each heat-wave day ranging from 12.1% to 61.3% [41]. Effects of high temperature and heat waves are greater in Mediterranean than North-Continental European cities [39-41]. Also cold temperatures are of concern for respiratory health, with a 3-4% increase in daily mortality and hospitalizations for respiratory causes in 75+ population for each degree Celsius decrease in minimum temperature or minimum apparent temperature. In this case, northern populations seem to be at greater risk than southern ones [42, 43]. Results from the available studies suggest an effect of heat and heat waves and
cold temperature on mortality, hospital admissions, admissions in geriatric units and emergency visits for specific respiratory diseases such as asthma and COPD and pneumonia although results are limited and somewhat contrasting and more evidence is needed [44].

Other weather conditions, i.e. specific variables such as humidity and rainfall, but also combinations of several meteorological variables (i.e. temperature, humidity, visibility, cloud cover, air pressure, wind speed) defined as “synoptic air masses” have been associated to increases in mortality and morbidity but specific evidence for respiratory causes is scanty and there is no clear evidence that these variables may have an independent effect apart from temperature [45-51].

**Synergy (effect modification) of air pollution and temperature effects**

Several European time-series and case-crossover studies have provided indirect evidence (i.e. that effects are stronger in the warm season or in warmer cities) suggestive of interactions between air pollution and heat, although other explanations are consistent with these results [52-55]. The multicentre APHEA study, found ozone effects on respiratory mortality only during summer [33], while single-city studies provided contrasting results, with a significant effect on respiratory deaths all year round [56], and a positive association on physician consultations for asthma and on pediatric asthma hospital admissions only in the summer months [57, 58]. A study in Cyprus showed an ozone effect on respiratory admissions stronger in the warm season [59].

The APHEA project provided also evidence of seasonal differences in the effect of pollutants other than ozone, i.e. black smoke and SO₂, whose effects on respiratory mortality were also found higher in summer [52]. Other studies found similar [54, 60], or contrasting findings [56, 58, 61]. The APHEA study provided evidence of effect modification not only by season but also according to typical temperatures for the area; the greatest PM10 effects were in the warmest cities but no result for respiratory causes was available [62]. On the other side of the relationship, a study from Greece found a greater effect of heat waves in Athens where pollution levels were higher than in all other urban areas [63].
Several studies provided consistent evidence of a synergy between the two exposures [63-76], with only one study showing no evidence of interaction [77]. In all these studies the potential interaction between air pollution health effects and high/low temperature was tested through interaction terms or by means of a stratified analysis in time series and case-crossover analyses. Among studies carried out in a European country (Table 2), three studies [54, 75, 78] analysed the synergistic effect on mortality for respiratory causes. In the study in UK, the ozone effect on respiratory mortality during hot days corresponded to a rate ratio of 1.009 while the pollutant had no effect on ordinary days (rate ratio=1.000), but the ozone-heat interaction was significant only in London and ozone-heat interactions were greatest in those aged <75 years [75]. In Italy, an effect of PM10 on respiratory mortality was found only for temperatures above the 50th percentile compared to no effect in days with temperature below the 50th percentile [54]. The study of Carder et al. [78] carried out in Scotland found instead a positive interaction between cold temperatures and black smoke concentrations on respiratory mortality. Other European studies analysed total mortality; they were focused on specific heat wave episodes [63-67] or on both warm and cold periods [68] and provided evidence of significant interaction between high temperature and pollutants, mainly ozone. Two multicentre studies suggest that the synergistic effect may vary among cities according to local climate characteristics, activity patterns and physical adaptation [67, 75].

The synergy between temperature and air pollution has been also evaluated in multicentre European studies analysing the other side of effect modification: air pollution levels modifying the health effect of temperature or heat waves (Table 3) [22, 79]. For ozone, there is consistent evidence of interaction with heat/heat wave effects on mortality for natural causes in the elderly but no evidence of interaction on respiratory mortality [22, 79]. Concerning PM10, the study before year 2000 did not find any interaction with temperature while the more recent time series studies showed a significant effect modification. In particular, PM10 significantly modified heat wave effect on mortality for respiratory causes in Mediterranean cities (65-74 yrs) [79] and there is a suggestion of interaction with effect of high temperature on this group of diseases. For PM10 there is also evidence of effect modification of temperature effect during cold season, with lower cold effect on respiratory mortality in high pollution days [22].
Overall, results about temperature-air pollution interactions suggest that this topic cannot be disregarded when studying temperature or air pollution effects regarding respiratory causes, since the true magnitude of the associations may be underestimated. Results differ by pollutant considered and study area, suggesting that the underlying mechanisms are driven by local conditions. Moreover, the evaluation of effect modification presents specific methodological challenges. In many studies stratification can provide quantitative estimates, but results are dependent on the selection of cut-offs for strata. On the other hand, the use of more flexible models, i.e. joint pollutant-temperature response surface on health outcomes, has the disadvantage to not provide parametric estimates [73].

Other weather conditions such as humidity have been suggested to interact with air pollutants effects. Low absolute humidity may increase the effect of total suspended particles (TSP) on hospitalizations for COPD [80]. However, it should be noted, that absolute humidity is very strongly correlated with temperature, so in essence this finding maybe reflecting temperature effects. Humidity was also found to be a significant effect modifier of the effect of air pollutants on mortality, as found in the 29 EU cities included in the APHEA2 project [62]; the observed effect of PM10 increased as humidity levels decreased. Another remarkable type of interaction is that from air masses and air pollutants. In a study in Birmingham, UK, two winter air masses associated with increased admission rates for respiratory causes (continental anticyclonic gloom and continental anticyclonic fine and cold) were also favourably associated with high PM10 levels [81].

**Air pollution and wildfires effects.**

Wildfire smoke is a complex mixture of particles, liquids and gaseous compounds. The effect of fires is usually measured respect to fine PM (PM2.5) levels since it predominates in the smoke [82-84], and is thought to be responsible of greater part of the observed health effects. Fine particles are created directly during the combustion process and also formed later from emitted gases through condensation and atmospheric chemical reactions [17]. During wildfires, levels of PM are usually well above the background pollution level for the area usually beyond air quality standard (24-h mean PM10: 50 µg/m³; 24-h mean PM2.5: 25 µg/m³), over 500 µg/m³ in some cases [17, 82-84]. The extreme event is identified according to a certain
threshold, i.e. the 99\textsuperscript{th} percentile of particulate distribution. This allows to distinguish extreme events from situations in which background pollution sources predominate.

Since wildfires are usually episodes of short duration, the length of the exposure may be too short to detect the health effects as well as to evaluate their impact on air quality [82-84]. As in the case of urban air pollution, during wildfire episodes the respiratory system is particularly affected: increases in mortality, hospitalizations, emergency visits for all respiratory causes and for specific diseases (mainly asthma, COPD, lower and upper respiratory diseases), asthma and COPD exacerbations, respiratory symptoms and decreases in lung function both in healthy subjects and in asthmatic and COPD patients [82-84]. Most evidence on short-term effects of wildfires comes from the US, Asia and Australia while only few studies have been carried out in the European context [85-88], despite the fact that wildfires are common in the Mediterranean forests of Greece, Spain, Italy and Portugal [16]. In the study carried out in Athens, Greece, the occurrence of a large forest fire (one which burnt more than 30 000 000 m\textsuperscript{2}), lead to significant short-term effect on mortality for respiratory causes in the elderly [85]; this effect could be explained only in part by an increase in ambient particle concentrations. A survey carried out in Barcelona, Spain during 2003 wildfires on healthy 6- to 19-year-old documented increased respiratory and eye symptoms with increasing frequency of wildfire smoke exposure; associations were stronger in subjects with lowest lung function [87]. Increases in hospital attendances for respiratory conditions and asthma have been documented during the fires which surrounded Vilnius in Lithuania in 2002 [88].

Studies on wildfire health effects commonly adjust for meteorological variables. Since during wildfire events ambient temperature is usually high, there is also a potential for interaction as demonstrated by the concomitance of heat wave and wildfire conditions in summer 2010 in Russia and the huge impact on population in terms of adverse effects on respiratory health [89]. This interaction could be explained, at the point of emissions, by changes in smoke constituents driven by temperature, sunlight, water vapour and interaction with other pollutants [17]. Furthermore, meteorological conditions influence smoke dispersion and transportation [19]. The long range transport of smoke plumes for thousands kilometres is a public health concern also in European countries as, for example, in Finland where long-range transported PM episodes originated from wildfires in Russia, Belarus, Ukraine and the Baltic countries.
are common [86]. However, no study to date has evaluated the possible effect modification of weather on PM related effects during wildfire. Other wildfire consequences include visibility impairment and ozone (O$_3$) generation [90]; also these factors may interact with PM levels in determining health effects [88].

Overall, the available evidence suggests an effect of wildfire on respiratory health. The greatest methodological challenge in these studies regards the estimate of exposure; in most cases PM measurements from air quality monitoring station are used but these are limited to specific points and therefore not well representative of actual exposure. The more recent approach of burnt areas from satellite data seems to be more effective in identifying areas at risk. Moreover, wildfires are rare events and effect depends also on the local context; therefore results are not easily generalizable and to date there is no consensus to estimate the exposure taking into account dispersion process of smoke [91].

**Air pollution and desert dust storms effects.**

Desertic regions throughout the world are known to be the source of dust storms that are driven by weather conditions and transported over long distance, with North Africa (Sahara) the main contributing area (over 50%) [92-94]. Dust particles derive from earth’s crust and affect air quality in particular PM10 and coarse particulates (PM2.5–10) levels [92-94]. For example, during Saharan events PM10 concentrations exceed EU daily limit value overcoming 100 µg/m$^3$ or 150 µg/m$^3$ at rural stations [59, 92, 94]. As wildfire smoke, also dust storms may be transported over thousands kilometers, changing composition and concentration of pollutants on the way and following specific trajectories that can be back-derived by mathematical models. These episodes can cause PM concentration peaks in areas with low local emissions also very far from the emission sources, including rural background areas [95].

The Mediterranean and Europe are particularly affected by dust storms from North Africa with significant impact on air quality and human health [92, 94]. The growing evidence in these regions suggests a greater effect of PM on dust days than in non dust days [59, 96-105], in particular on mortality or hospital admissions for respiratory causes [97, 98, 100-105] (Table 4). On the contrary, no effect was found in a study in Cyprus [59], while a greater effect on non dust days was found in Athens.
Overall, associations are more coherent regarding coarse particles (PM2.5-10) than for PM2.5 and PM10. Only studies outside Europe, mainly from Asia and Australia, evaluated dust storms effects on specific respiratory diseases, such as pneumonia, rhinitis, COPD and asthma; however, evidence is still limited and rather contrasting especially regarding hospital admissions for these diseases [92, 94].

As in the case of wildfires, the meteorological context is important also in the case of dust storms; cyclone and anticyclone systems may favour the long-range transport of dust and convective activity and rainfalls cause the abatement of dust air masses [95]; in addition, dust storms tend to occur in contemporary with high ambient temperatures and high ozone levels [94]. Despite these important links, the interaction between weather variables and dust storms has not been analysed yet. However, the effect modification of particulates by Saharan dust days was robust both to ozone adjustment and to the exclusion of extremely warm days [98]. To the best of our knowledge, only one study have quantified the direct health effect of dust storms on health providing evidence for an increase in asthma and respiratory admissions especially in younger population [106].

The study of the effect of dust storms presents specific methodological challenges [92, 94]. First, the low frequency of dust days restricts analysis of cause-specific mortality or morbidity. Moreover, for their nature the occurrence and intensity of dust intrusions is strongly linked to the specific local context. For example, Saharan dust storms mostly affect the Eastern Mediterranean Basin regions and their frequency, intensity, seasonality, as well as years considered and local climate conditions affect the dust composition and consequently health effects. Similarly to wildfires, the definition of dust event is critical. Usually dust days are defined based on overcome of a specific threshold of PM, or on the basis of back-trajectory analysis, considered to be a marker of dust transport from the source regions. In urban areas dust events may be underestimated due the presence of other sources of dust mainly anthropogenic [94].

**Mechanisms and vulnerable subgroups**

The respiratory system is the main target of gases, aerosols and particles present in air pollution. A wide range of effects on the respiratory system are triggered by environmental toxicants, from reversible local responses to long-term chronic effects:
local irritation, direct cellular damage on epithelium of respiratory airways, allergic responses (i.e. asthma), cancer. The underlying mechanisms are different for the different pollutants. Ozone provokes an oxidative damage to the respiratory epithelium resulting in lung inflammation, decrements in lung function, worsening of respiratory tract symptoms and increased airway reactivity [107]. Particulate matter, via enhanced oxidative stress, may disrupt lung endothelial cell barrier integrity, thereby inducing lung dysfunction and adverse cardiopulmonary outcomes [108].

Not only air pollution but also high and low temperatures have a strong effect on respiratory health as seen above (see paragraph “Outdoor temperature”). Underlying mechanisms are better known for cold than for heat. Cold temperature may affect respiratory health in different ways and seem to affect not only susceptible but also healthy subjects. Breathing cold air causes the cooling of nasal and bronchial mucosa seriously impairing ciliar motility and consequently reducing immune system’s resistance to respiratory infections [109, 110]. Exposure to cold air may also increase the number of granulocytes and macrophages in the lower airways in healthy subjects [111] and induce bronchoconstriction [112, 113] suggesting that cold exposure could be involved in the pathogenesis of the asthma-like condition. Part of the increase in respiratory outcomes during cold periods may also be attributed to cross-infections from increased indoor crowding during winter [114].

In contrast to observed cold-related effects, the health consequences deriving from exposure to heat seem to be greater in patients affected by chronic respiratory diseases. In these patients, it may be hypothesized that thermoregulatory responses to heat stress, particularly those involving the respiratory system, may be uneffective to dissipate excess heat thus increasing their risk to developing heat stress conditions such as dehydration and heatstroke. However this hypothesis is still not supported by experimental studies [115]. A different pathway linking heat exposure to respiratory health outcomes involves the clinical course of heat-related illnesses such as heatstroke. In patients with heat stroke, an acute lung inflammation and damage might occur [116] and heat may trigger a series of physiological changes in the lung leading to a severe respiratory distress syndrome [117, 118]. Recent experimental evidence suggests that chronic heat stress exposure could increase the susceptibility of animals to the highly pathogenic respiratory viruses by reducing local immunity in the respiratory tract, i.e. the number of pulmonary alveolar macrophages [119]. Other weather conditions, particularly humidity, may adversely affect respiratory
health but their role is still unclear. Some studies showed that in both healthy and asthmatic subjects humidity may decrease lung capacity and increasing airways resistance [120, 121] while in others humidity did not influence non-specific airway hyperresponsiveness [122]. Humidity may also indirectly affect respiratory allergic diseases by influencing atmospheric levels of aeroallergens, with low humidity favouring release, dispersion and transport of pollen [123, 124]. Extreme weather events such as thunderstorms may trigger asthma epidemics by inducing pollen grain rupture by osmotic shock that releases respirable allergens into the atmosphere [123, 124].

The above mentioned evidence of a synergistic effect between air pollution and temperature can have different explanations. Since the respiratory surfaces are the primary route by which air pollutants enter the body, the activation of thermoregulatory responses at pulmonary level during prolonged heat exposure may augment the total intake of airborne pollutants due to the increase in ventilation rate and lung volumes [125, 126]. It has also been suggested that variations in the sources of air pollution and meteorological factors can result in changes in characteristics of the air pollution mixture across seasons [68, 127, 128]. However, in an experimental study modifications in PM components were not able to explain the seasonal difference in PM effects that could instead be related with the highest prevalence of allergens in spring and summer influencing the onset and severity of allergic diseases [129]. The higher effects of pollutants observed in summer than in winter might also be due to the lower exposure measurement error during summer as a consequence of more time spent outdoors or, especially for particles, due to a more similar composition between indoor and outdoor pollutants [54, 68, 127, 130, 131].

Another hypothesis is that the lower winter mortality for infectious diseases resulting in a lower mortality among the elderly, i.e. among those most susceptible, has the consequence of a larger pool of susceptible people at risk of air pollution effect in the following summer [68, 127, 130]. To explain the interaction between pollutant and low temperature [78], a hypothesized mechanism is that the cold-related impairment of respiratory mucociliary function may inhibit the clearance of pollutants [109, 110]. Meteorological factors such as temperature may also influence the interaction between allergens and air pollution in producing respiratory adverse effects since air pollution-related damage on respiratory epithelium increases airway permeability stimulating allergen-induced responses and absorption of pollutants to the surface of pollen grains.
may modify their allergenic potential [123, 124]. Also humidity may modify air pollution effect on respiratory health. Airways of individual suffering from respiratory diseases seem to be protected against the effect of particles by high humidity probably due to the reduced number of particles [80].

Mechanisms explaining the respiratory effects of wildfires and dust storms are mainly linked with air pollution associated to these events. Particulate matter is the predominant air pollutant in fire smoke that contains also gases including carbon monoxide, nitrous oxides, polycyclic aromatic hydrocarbons, VOCs, ozone and nitrous dioxide [82-84]. Wood smoke particles have been shown to activate systemic and pulmonary inflammation in healthy human subjects [92, 94]. There is still insufficient evidence to establish whether wildfire PM10 may have a greater effect than urban background PM10 [17, 82-84]. However, smoke particulate is probably different in composition respect to urban PM, having a greater concentration of PM10 that can accumulate in the lungs. An in vivo experiment found that responses to wood smoke consist in higher inflammatory and cytotoxic responses than those triggered by urban particulate matter [82]. Apportionment techniques are expected to provide important insights to whether fire components are less or more toxic than the same constituents from fossil fuel burning and to clarify the underlying mechanisms.

In the case of dust storms, not only the chemical composition of particles but also its biological content is the probable causative agent of respiratory health effects [92-94]. In particular, coarse particles may have a greater allergenic and inflammatory property, absorbing to their surface pollens and microorganisms such as bacteria and fungi, as well as endotoxins, which are components of the bacterial wall that can cause respiratory and systemic inflammatory responses, and exacerbate lung disease [92-94]. This hypothesis is coherent with recent evidence of an increase in infectious diseases (i.e. meningitis) in dust days [94]. Moreover, in their long-range travel dust particles may absorb metals, pesticides and industrial products mixing with anthropogenic emissions of industrial regions (e.g.: North African); Inhaling these compounds can cause lungs irritation, reducing lung capacity through activating oxidative stress pathways [92, 94]. As in the case of wildfires, chemical speciation and toxicity studies may clarify whether dust particles are more or less toxic than
urban PM, considering also that dust may be one of the component of PM itself other than interact with it.

Vulnerable subgroups
The links between climate and air pollution on human health are complicated by the presence in a population of specific subgroups at greater risk of adverse health effects (i.e. vulnerable subgroups) owing to a series of environmental, individual and population characteristics. According to the Intergovernmental Panel on Climate Change, vulnerability is defined as a function of the level of exposure (character, magnitude and rate of weather event), of the level of the susceptibility and the adaptive capacity of populations [132]. Several climate-sensitive subgroups have been identified: heat and heat waves have a stronger impact on people with impaired physiological and behavioural responses to heat due to age, gender, socio-economic factors, pre-existing chronic diseases, use of certain medications and environmental conditions (i.e. lack of air conditioning) but the pattern of susceptibility factors is population-specific and may vary over time [115, 133]. Regarding cold exposure, indoor climatic conditions seem to confer a greater vulnerability especially in the elderly [134, 135], while there is contrasting evidence of socioeconomic gradient of risk [136, 137]. Less known are the susceptibility factors to other extreme events like wildfires and dust storms. Subjects with asthma and COPD, women and children are more likely to be affected by wildfires [17, 82-84]; children, elderly, people of low income and persons with cardiovascular and respiratory disease may be more susceptible to dust storms [92-94]. On the other hand, individual characteristics to identify subgroups at greater risk due to air pollution are pollutant-specific. Susceptible subjects to particulate matter comprise elderly, people of low socioeconomic status and COPD and cardiovascular disease patients [138, 139], while regarding ozone there is contrasting evidence on whether some subgroups have a greater risk of adverse effects than the general population [140, 141].

Research needs in the context of respiratory health
Considering climate change scenarios, to quantify the effect estimates on respiratory health and to identify vulnerable population subgroups are crucial research areas to carry out health impact assessments to understand future impacts and to support
decision-makers and health care community in the fight against this global environmental threat [6].

Table 5 summarizes for each climate hazard the main respiratory outcomes and the population subgroups for which there is evidence of association from epidemiological studies; research gaps and future expected impacts under climate change are also pointed out. Overall, every climate hazard appears to have a significant impact on the respiratory system, although evidence on specific respiratory diseases and specific age groups is still limited. At European level, there is scarce epidemiological evidence about cold extremes and wildfires effects. Multicentre studies are lacking in the analysis of rare and local-extent episodes such as dust storms and wildfires. The ongoing PHASE (www.hpa.org.uk/Topics/EmergencyResponse/ExtremeWeatherEventsAndNaturalDisasters/PHASE/) and MEDPARTICLES (www.epidemiologia.lazio.it/medparticles/index.php/en/) multicenter projects will provide further insights on both these hazardous exposures. Pre-existing respiratory diseases are important vulnerability factors to both temperature and air pollution effects. Since vulnerability factors are specific for each climate hazard and may vary across populations and over time, more research is needed, in particular on younger age groups and children, but also on other population segments as low socioeconomic groups.

Considering future impacts on respiratory diseases, population aging, increased prevalence of chronic diseases and the socioeconomic transitions which are currently ongoing in several countries the portion of population at risk will probably increase [142, 143]. Almost all climate hazards will worsen under climate change, and as much the related disease burden. The only beneficial effect will consist in the reduction of cold-related effect (i.e. respiratory infections) due to warmer winters [143]. However, due to the complexity of the above mentioned climate-air quality interactions, a great deal of uncertainty remains regarding future trends of climate and pollutants and research is needed to increase the modelling capability to better understand the interplay between human activities, air pollution and regulatory requirements, climate policy, economic factors, and to predict future trends of air pollutants, accounting for uncertainty and variability in projections of global change. Advances in modelling capability can derive from disease surveillance integrated with air pollution, weather
and climate data and from combining ecological approaches (time series studies) with spatial methods to produce a more complete evaluation of health effects taking into account both geographical and temporal variations. From a public health point of view, since health professionals have joined late the climate change debate [144], they are urged to develop modelling skills in relation to climate change, particularly by combining climate models with ecological and health outcome models for projecting disease dynamics under various climate scenarios.

**Policy implications**

Due to the close climate and air pollution inter-linkages, climate change policies need to be integrated with air quality policies to be effective. Moreover, mutual benefits can be achieved: actions to mitigate climate change by reducing greenhouse gases emissions may help in reducing air pollution since they involve main changes in transport and energy sectors which are also driving pollutant sinks and, at the same time, clean air measures can reduce anthropogenic emissions that are important contributors to global warming. Cobenefits of climate policies on air pollution have been evaluated for Europe [145]. Although limitations in data availability, especially in relation to the scenario datasets and modelling uncertainties, cobenefits resulted for all investigated emission scenarios, with the scenarios based on energy efficiency strategies leading to larger cobenefits [145].

At the European level, although stringent emission targets have been made (i.e. to reduce the domestic GHG emissions by 80 percent by 2050 compared to 1990 levels), the greatest reductions in GHG emissions have been achieved only as an indirect effect of the current economic crisis [146]. To accomplish GHG reductions targets, countries need to reach the convergence between resource productivity and efficiency. However, energy efficiency improvements, i.e. switching to fuel with a low-carbon content but higher price, lead to increases in environmental inequality posing the major risks to disadvantage groups, for example due to inadequate housing and heating systems. To cope with economic and climate changes, European countries need to develop a more comprehensive policy framework that integrates climate policy, industrial policy, employment and social policy [146].

**Conclusions**
Climate and climate change are modifying air pollution effects on respiratory health in several ways: climate variations are predicted to influence the start, duration and intensity of the pollen season, to increase the frequency and intensity of heat waves, heavy precipitation events (i.e. thunderstorms) and wildfires and to raise long-range transport of air pollutants and allergens [4].

To face both the current and future climate and pollution challenges, adequate policy and public health actions are needed, taking into account the interrelations between the two hazardous exposures. Since climate change is a global problem with the worst consequences occurring not in developed but in developing countries, global actions are needed. Policies to reduce greenhouse emissions need to be established especially in countries which hold the greatest emission burden. In parallel, developing countries are increasingly affected by urban air pollution due to the rapid economic and population growth [147, 148]. The way forward to face both these challenges needs the multisectorial collaboration of epidemiologist, climatologist, respiratory and allergy specialists, policy makers, public health professionals that share the heavy responsibility to guide world through the climate crisis and make the environment sustainable for future generations.

Acknowledgments
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Figure 1. Climate change, its influence on extreme weather events, air pollution and aeroallergens, and effects on respiratory health.
CLIMATE CHANGE

Changes in local weather patterns (i.e. temperature, precipitation)
Changes in frequency of extreme weather events (i.e. heatwaves, wildfires, dust storms)

Changes in atmospheric concentration of pollutants
O$_3$, PM, SO$_2$, NO$_2$, CO

weather-pollutant interaction

Effects on respiratory health:
- Premature mortality
- Allergic responses
- Exacerbations of chronic respiratory diseases (i.e. asthma, COPD)
- Occurrence of respiratory diseases
- Declines in lung function
- Lung cancer

Changes in aeroallergens

allergen-pollutant interaction

weather-allergen interaction
Table 1. Multicentre time-series studies of short-term effects of heat, cold and heat waves on respiratory health in Europe.

<table>
<thead>
<tr>
<th>Exposure</th>
<th>EU Project</th>
<th>Reference</th>
<th>Number of cities</th>
<th>Population</th>
<th>Temperature indicator (°C)</th>
<th>Health indicator</th>
<th>% change per 1°C increase in Temperature indicator or during heat wave days (95% CI)*</th>
<th>Lag</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heat</td>
<td>PHEWE</td>
<td>Baccini 2008 [39]</td>
<td>15</td>
<td>all ages</td>
<td>Tappmax threshold: 29.4 Mediterranean cities; 23.3 North-Continental cities</td>
<td>Respiratory deaths</td>
<td>6.7% (2.4, 11.3%) Mediterranean cities; 6.1% (2.5, 11.1%) North-Continental cities</td>
<td>Lag 0-3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Baccini 2008 [39]</td>
<td>75+ yr</td>
<td>75+ yr</td>
<td>23.3 North-Continental cities</td>
<td></td>
<td>8.1% (3.2, 13.4%) Mediterranean cities; 6.6% (3.0, 11.4%) North-Continental cities</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Michelozzi 2009 [40]</td>
<td>12</td>
<td>all ages</td>
<td>Tappmax 90th percentile (range): 19.7, 36.4</td>
<td>Respiratory admissions</td>
<td>2.1% (0.6, 3.6%) Mediterranean cities; 1.2% (0.1, 2.2%) North-Continental cities</td>
<td>Lag 0-3</td>
<td></td>
</tr>
<tr>
<td>Heat wave</td>
<td>EuroHEAT</td>
<td>D’Ippoliti 2010 [41]</td>
<td>7</td>
<td>65-74 yr</td>
<td>Tappmax 90th percentile (range): 27.1, 39.9*</td>
<td>Respiratory deaths</td>
<td>32.4% (14.3, 53.3%) males; 45.8% (22.3, 73.7%) females - Mediterranean cities; 16.8% (6.3, 28.1%) males; 12.6% (-0.1, -27.0%) females - North-Continental cities</td>
<td>no lag</td>
</tr>
<tr>
<td></td>
<td></td>
<td>D’Ippoliti 2010 [41]</td>
<td>75-84 yr</td>
<td>75-84 yr</td>
<td></td>
<td></td>
<td>44.8% (30.9, 60.0%) males; 61.3% (44.3, 80.4%) females - Mediterranean cities; 19.0% (11.0, 27.6%) males; 21.4% (12.9, 30.6%) females - North-Continental cities</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>D’Ippoliti 2010 [41]</td>
<td>85+ yr</td>
<td>85+ yr</td>
<td></td>
<td></td>
<td>58.9% (42.9, 76.5%) males; 58.1% (44.3, 73.3%) females - Mediterranean cities; 12.1% (3.5, 21.4%) males; 30.0% (22.8, 37.6%) females - North-Continental cities</td>
<td></td>
</tr>
<tr>
<td>Cold</td>
<td>PHEWE</td>
<td>Analitis 2008 [42]</td>
<td>15</td>
<td>all ages</td>
<td>Tappmin median (range): -5.3, 11.1</td>
<td>Respiratory deaths</td>
<td>2.8% (1.6, 4.0%) Mediterranean cities*; 3.7% (2.9, 4.5%) North-Continental cities*; 3.1% (2.1, 4.1%)°; 3.5% (2.8, 4.3%)°; 3.3% (2.6, 4.1%)°</td>
<td>Lag 0-15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Analitis 2008 [42]</td>
<td>15-64 yr</td>
<td>15-64 yr</td>
<td></td>
<td></td>
<td>3.1% (2.1, 4.1%)°; 3.5% (2.8, 4.3%)°; 3.3% (2.6, 4.1%)°</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Analitis 2008 [42]</td>
<td>65-74 yr</td>
<td>65-74 yr</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Analitis 2008 [42]</td>
<td>75+ yr</td>
<td>75+ yr</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Marino 2009 [43]</td>
<td>12</td>
<td>all ages</td>
<td>Tmmin mean (range): -0.9, 13.7</td>
<td>Respiratory admissions</td>
<td>-1.6% (-2.5, -0.6%) Mediterranean cities; -2.5% (-3.6, -1.3%) North-Continental cities; -2.7% (-3.3, -2.1%) Mediterranean cities; -4.1% (-5.7, -2.5%) North-Continental cities</td>
<td>Lag 0-15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Marino 2009 [43]</td>
<td>75+ yr</td>
<td>75+ yr</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


* 90%CI in D’Ippoliti et al. 2010 [41]
° % increase per 1°C decrease in Temperature indicator
^ study period except summer 2003
### Table 2. Interaction of weather variables on air pollution effects: epidemiological studies in European cities published since ‘90s.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Country period</th>
<th>Study design</th>
<th>Population</th>
<th>Health indicator</th>
<th>Method to detect interaction</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pattenden 2010</td>
<td>15 conurbations (UK) &lt;br&gt; Summer 1993-2003</td>
<td>Time-series</td>
<td>All ages</td>
<td>Mortality (total and specific causes)</td>
<td>Interaction terms</td>
<td>Positive interaction of ozone and high temperature, significant only in London</td>
</tr>
<tr>
<td>Carder 2008</td>
<td>Scotland (3 cities) &lt;br&gt; 1981-2001</td>
<td>Time-series</td>
<td>All ages</td>
<td>Mortality (total and specific causes)</td>
<td>Interaction terms</td>
<td>No evidence of effect modification by season. Significant positive interaction of black smoke and low temperature on RESP causes</td>
</tr>
<tr>
<td>Stafoggia 2008</td>
<td>Italy (9 cities) &lt;br&gt; 1997-2004</td>
<td>Case-crossover</td>
<td>35+ yrs</td>
<td>Mortality (total and specific causes)</td>
<td>Interaction terms; stratification by temperature</td>
<td>Significant positive interaction of PM10 and summer/high temperatures for natural/CVD; heterogeneity for RESP causes</td>
</tr>
<tr>
<td>Nawrot 2007</td>
<td>Flanders (Belgium) &lt;br&gt; 1997-2003</td>
<td>Time-series</td>
<td>All ages</td>
<td>Mortality (total and specific causes)</td>
<td>Stratification by season/temperature</td>
<td>Significant positive interaction of PM10 and summer for natural, CVD and RESP causes. Interaction between PM10 and high temperature on effect on total mortality</td>
</tr>
<tr>
<td>Filleul 2006</td>
<td>France (9 cities) &lt;br&gt; Summer 2003</td>
<td>Time-series</td>
<td>All ages</td>
<td>Mortality (total)</td>
<td>Joint response surfaces</td>
<td>Positive interaction of ozone and high temperature heterogeneous among cities</td>
</tr>
<tr>
<td>Dear 2005</td>
<td>France (12 cities) &lt;br&gt; Summer 2003</td>
<td>Episode analysis</td>
<td>All ages</td>
<td>Mortality (total)</td>
<td>Interaction terms</td>
<td>Significant positive interaction of ozone and high temperature</td>
</tr>
<tr>
<td>Sartor 1995, 1997</td>
<td>Belgium, Summer 1994</td>
<td>Episode analysis</td>
<td>65+ yrs</td>
<td>Mortality (total)</td>
<td>Stratification by temperature</td>
<td>Significant positive interaction of ozone and high temperature at levels &gt;20°C</td>
</tr>
<tr>
<td>Katsouyanni 1993</td>
<td>Athens (Greece) &lt;br&gt; Summer 1987</td>
<td>Episode analysis</td>
<td>All ages</td>
<td>Mortality (total)</td>
<td>Interaction terms</td>
<td>Significant positive interaction of SO2 and high temperature; suggestive interaction for ozone and smoke</td>
</tr>
</tbody>
</table>

RESP: respiratory  
IHD: ischemic heart disease  
CVD: cardiovascular  
CP: cardiopulmonary (total cardiovascular and respiratory causes)  
ED: Emergency Department  
EC: Elemental carbon  
* Time-series classification and regression tree model  
CHF: congestive heart failure
Table 3. Interaction of air pollution on heat/heat waves-related effects: evidence from European studies.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Country period</th>
<th>Study design</th>
<th>Population</th>
<th>Health indicator</th>
<th>Method to detect interaction</th>
<th>Results</th>
</tr>
</thead>
</table>
| Katsouyanni 2009 [22] | 15 EU cities summer 1990-2000   | Time-series of temperature          | All ages   | Mortality (total and specific causes) | stratification by air pollution | Ozone: significant positive interaction with temperature on total mortality: 1.66% vs 2.10% (all ages) (fixed effects model)  
Black smoke: significant positive interaction with temperature on CVD mortality  
Katsouyanni 2009 [22] | 10 EU cities summer 1990-2004   | Time-series of temperature and heat wave days | All ages   | Mortality (total and specific causes) | stratification by air pollution | PM10: significant positive interaction with high temperature on all causes and CVD (0-64 yrs, 65+ yrs); suggestion of positive interaction for RESP mortality.  
Ozone: significant positive interaction with high temperature on all causes. No significant interaction with CVD and RESP.  
NO2: no significant interaction  
No evidence of interaction between pollutant and heat wave effect  
Analitis 2012 [79]   | 9 EU cities summer 1990-2004    | Time-series of heat wave days       | All ages   | Mortality (total and specific causes) | stratification by air pollution | Ozone: significant positive interaction with heat waves in North-Continental cities for natural causes (all ages) and CVD (all ages, 75-84 yrs); no significant interaction for RESP.  
PM10: significant positive interaction with heat waves for natural causes and CVD (all ages, 75-84, 85+) and for RESP in Mediterranean cities (65-74 yrs) |
<table>
<thead>
<tr>
<th>Reference</th>
<th>Country</th>
<th>Study design</th>
<th>Population</th>
<th>Health indicator</th>
<th>Method to detect interaction</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midlleton 2008 [59]</td>
<td>Nicosia (Cyprus) 1995-2004</td>
<td>Time-series</td>
<td>All ages</td>
<td>Hospital admissions (total and specific causes)</td>
<td>Stratification by dust days and PM quartiles</td>
<td>The effects of PM10 on dust-storm days on all-cause and cardiovascular admissions was comparable to the effects seen on non-storm days with the highest PM10 levels. No significant effect on respiratory admissions.</td>
</tr>
<tr>
<td>Perez 2008 [96]</td>
<td>Barcelona (Spain) 2003-2004</td>
<td>Case-crossover</td>
<td>All ages</td>
<td>Mortality (total causes)</td>
<td>Stratification by dust days; interaction terms</td>
<td>Effect of PM10-2.5 greater during dust days compared with non dust days. No evidence of interaction for PM2.5.</td>
</tr>
<tr>
<td>Jimenez 2010 [97]</td>
<td>Madrid (Spain) 2003-2005</td>
<td>Time-series</td>
<td>All ages</td>
<td>Mortality (total and specific causes)</td>
<td>Stratification by dust days; interaction terms</td>
<td>Effects of PM10 only on dust days, on all-cause, cardiovascular and respiratory mortality; no effect of PM2.5 or PM10-2.5 on dust days.</td>
</tr>
<tr>
<td>Mallone 2011 [98]</td>
<td>Rome (Italy) 2001-2004</td>
<td>Case-crossover</td>
<td>All ages</td>
<td>Mortality (total and specific causes)</td>
<td>Stratification by dust days; interaction terms</td>
<td>Effect of PM10-2.5 greater during dust days compared with non dust days for all causes and cardiac causes and diseases of circulatory system; suggestion of positive interaction on respiratory causes. Positive interaction of PM10 with dust days on cardiac mortality. No evidence of interaction for PM2.5.</td>
</tr>
<tr>
<td>Samoli 2011a [99]</td>
<td>Athens (Greece) 2001-2006</td>
<td>Time-series</td>
<td>All ages</td>
<td>Mortality (total and specific causes)</td>
<td>Stratification by dust days; interaction terms</td>
<td>Effect of PM10 higher in non dust days and essentially null effects during dust days; significant interactions except for respiratory and cardiovascular causes among those &lt;75 years</td>
</tr>
<tr>
<td>Samoli 2001b[100]</td>
<td>Athens (Greece) 2001-2006</td>
<td>Time-series</td>
<td>All ages</td>
<td>Pediatric asthma emergency admissions</td>
<td>Stratification by dust days; interaction terms</td>
<td>Effects of PM10 greater on dust days compared with non dust days</td>
</tr>
<tr>
<td>Tobias 2011 [101]</td>
<td>Madrid (Spain) 2003-2005</td>
<td>Case-crossover</td>
<td>All ages</td>
<td>Morbidity (total causes)</td>
<td>Stratification by dust days; interaction terms</td>
<td>Effect of PM10-2.5 greater during dust days compared with non dust days for all causes. No evidence of interaction for PM2.5.</td>
</tr>
<tr>
<td>Zauli Sajani 2011 [102]</td>
<td>Emilia-Romagna region (Italy) 2002-2006</td>
<td>Case-crossover</td>
<td>All ages</td>
<td>Mortality (total and specific causes)</td>
<td>Stratification by dust days; interaction terms</td>
<td>Evidence of increased respiratory mortality on dust days in hot season in 75+ yrs old, although interaction was not significant. No evidence of effect modification for any season for natural and cardiovascular mortality.</td>
</tr>
<tr>
<td>Alessandrini 2012 [103]</td>
<td>Rome (Italy) 2001-2004</td>
<td>Case-crossover</td>
<td>All ages</td>
<td>Morbidity (total and specific causes)</td>
<td>Stratification by dust days; interaction terms</td>
<td>Effect of PM10-2.5 greater during dust days compared with non dust days for respiratory causes; suggestion of positive interaction of PM10 on cerebrovascular causes.</td>
</tr>
<tr>
<td>Diaz 2012 [104]</td>
<td>Madrid (Spain) 2003-2005</td>
<td>Case-crossover</td>
<td>All ages</td>
<td>Morbidity (total and specific causes)</td>
<td>Stratification by dust days; interaction terms</td>
<td>Effect of PM10 greater during dust days compared with non dust days for respiratory causes during cold season,</td>
</tr>
<tr>
<td>Study</td>
<td>Location</td>
<td>Study Design</td>
<td>Age Group</td>
<td>Outcome Measures</td>
<td>Methods</td>
<td>Findings</td>
</tr>
<tr>
<td>------------</td>
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<td>--------------</td>
<td>-----------</td>
<td>------------------------------------------------------</td>
<td>----------------------------------------</td>
<td>-----------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Perez 2012</td>
<td>Barcelona (Spain) 2003-2007</td>
<td>Case-crossover</td>
<td>All ages</td>
<td>Mortality (total and specific causes)</td>
<td>Stratification by dust days; interaction terms</td>
<td>Effect of PM10-2.5 greater during dust days compared with non dust days for cardiovascular causes; suggestion of positive interaction of PM2.5 during dust days for cardiovascular and respiratory mortality</td>
</tr>
<tr>
<td>Thalib 2012</td>
<td>Kuwait 1996-2000</td>
<td>Time-series</td>
<td>All ages</td>
<td>Respiratory and asthma hospital admissions</td>
<td>Stratification by dust days</td>
<td>Evidence of greater risk for asthma admission in &lt;15 yrs and all ages during the dust days compared with non dust days (lag 0); not significant for older age groups. Effect on respiratory admissions in &lt;15yrs, 15-64 yrs, all ages. No effect on 65+ yrs old.</td>
</tr>
</tbody>
</table>
### Table 5. Synthesis of evidence on respiratory outcomes by climate hazard: vulnerable subgroups, research gaps and future impacts

<table>
<thead>
<tr>
<th>Climate hazard</th>
<th>Study outcomes</th>
<th>Study population groups</th>
<th>Research gaps</th>
<th>21st century impacts under climate change scenarios</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High temperature/heat waves</strong></td>
<td>All respiratory diseases (mortality, HA)</td>
<td>Children, adult, elderly</td>
<td>- Effect on specific diseases/morbidity outcomes</td>
<td>Increase in effects due to the higher frequency of hot extremes and heat waves</td>
</tr>
<tr>
<td></td>
<td>Pneumonia (mortality, HA, geriatric admissions)</td>
<td>Adult, elderly</td>
<td>- Effect on children and young age groups</td>
<td>Reduced effects due to change in adaptive capacity of populations</td>
</tr>
<tr>
<td></td>
<td>COPD (mortality, HA)</td>
<td>Elderly</td>
<td>- Effect on low socio economic subgroups</td>
<td>Increasing in vulnerable population due to aging, also in developing countries</td>
</tr>
<tr>
<td></td>
<td>Asthma (mortality, HA, prevalence)</td>
<td>Children, adult</td>
<td>- Short and long-term harvesting effect</td>
<td>Increasing in vulnerable population due to increasing prevalence of chronic respiratory diseases in industrialized countries</td>
</tr>
<tr>
<td><strong>Cold temperature/cold spells</strong></td>
<td>All respiratory diseases (mortality, HA, GPs visits)</td>
<td>Children, adult, elderly</td>
<td>- Population health impacts</td>
<td>Change in heat-related effects in different socio-economic scenarios</td>
</tr>
<tr>
<td></td>
<td>Lower respiratory tract disease (mortality, GPs visits)</td>
<td>Elderly</td>
<td>- Pathogenetic mechanisms</td>
<td>Increase in infectious diseases in children under 5 in developing countries</td>
</tr>
<tr>
<td></td>
<td>Asthma (ED visits, GPs visits)</td>
<td>Children, adult</td>
<td>- Increase in effects due to the higher frequency of hot extremes and heat waves</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Upper respiratory tract disease (GPs visits)</td>
<td>Elderly</td>
<td>- Reduced effects due to change in adaptive capacity of populations</td>
<td></td>
</tr>
<tr>
<td><strong>Wildfires</strong></td>
<td>All respiratory diseases (mortality, HA/rehospitalization, GPs visits, ED visits)</td>
<td>Children, elderly</td>
<td>- Increasing in vulnerable population due to aging, also in developing countries</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Asthma (ED visits, outpatient attendance, decreases lung function, asthma symptoms)</td>
<td>Children, adults, asthmatics</td>
<td>- Increasing in vulnerable population due to prevalence of chronic respiratory diseases in industrialized countries</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Upper respiratory tract disease (outpatient attendance, respiratory symptoms)</td>
<td>Children</td>
<td>- Evidence from multicentre studies</td>
<td></td>
</tr>
<tr>
<td></td>
<td>COPD (ED visits, HA, exacerbation of symptoms)</td>
<td>Adult, elderly, COPD patients</td>
<td>- Interaction with urban air pollution</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lower respiratory tract disease (hospital admissions, emergency room visits)</td>
<td>Children, elderly</td>
<td>- Interaction with heat waves</td>
<td></td>
</tr>
<tr>
<td><strong>Dust storms</strong></td>
<td>All respiratory diseases (mortality, HA, ED visits)</td>
<td>Children, adult, elderly</td>
<td>- Population health impacts</td>
<td></td>
</tr>
<tr>
<td></td>
<td>COPD (ED visits, HA)</td>
<td>Elderly</td>
<td>- Pathogenetic mechanism</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Asthma (mortality, pediatric admissions, HA, ED visits, decreases lung function, asthma exacerbations)</td>
<td>Children, adults, asthmatics</td>
<td>- Evidence from multicentre studies</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pneumonia (HA)</td>
<td>Children, adult, elderly</td>
<td>- Evidence from studies in areas most exposed</td>
<td></td>
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<tr>
<td></td>
<td>Rhinitis (HA, clinical visits)</td>
<td>Children</td>
<td>- To identify vulnerability factors</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>- Interaction with weather conditions</td>
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<td></td>
<td>- Effect of consecutive days of dust storms</td>
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<td></td>
<td></td>
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<td>- Evidence particles chemical composition</td>
<td></td>
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<tr>
<td>Temperature-pollutant interaction</td>
<td>All respiratory diseases (mortality, HA, ED visits)</td>
<td>Adult, elderly</td>
<td>Interaction between air pollutants and cold temperature</td>
<td>Interaction of temperature on specific pollutants</td>
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<tr>
<td></td>
<td>Asthma (ED visits)</td>
<td>Children</td>
<td>Population health impacts</td>
<td>Toxicological and pathogenetic mechanisms</td>
</tr>
</tbody>
</table>

HA: Hospital admissions  
ED: Emergency Room  
GPs: General Practitioners  
COPD: Chronic Obstructive Pulmonary Disease