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SCIENTIFIC PAPER

THE MUTUAL INFLUENCES OF MAN-MADE POLLUTANTS AND ALLERGIC MANIFESTATIONS

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Abstract: *The United Nations have projected the world population to reach 9.6 billion by 2050 and that, by then, over 50% of the world population will be living in urban areas. This continuing population growth and accompanying urbanization lead to serious concerns about clean water and food for all, but also about climate change and pollution. Soil and water pollution are directly affecting the crops grown for consumption, and air pollution is affecting our mucosal barriers in the respiratory and gastro-intestinal tract on a daily basis. This review provides an overview of the different types of pollution, and the health effects triggered by especially air pollution ranging from heart disease, pulmonary disease, cancer, to fatal respiratory infections. In addition, the differences in how pollution-induced effects are affecting different age-groups are discussed. Finally, the socio-economic causes and consequences (e.g. Quality of Life and Years of Life Losses versus medical care cost) of these pollution-induced diseases are debated.*

Keywords: *air pollution, urban environment, allergy, asthma, socio-economic costs*

1. Global urbanization and man-made pollution

1.1. Urbanization

Around 10.000 BC, the first hunter-gatherers started to live in villages near which they grew their crops and housed their livestock (Pain, 2016). Pain paints the transition of these early villages into the urban situation we live in nowadays, addressing both the benefits as well as the risks of this way of living. In 1950, 30% of the world's population was urban, whereas it is anticipated that by 2050, 66% of the world's population will be urban (United and Nations, 2014). This growing urbanization leads to serious concerns about climate change, pollution and the demands for clean water, food and energy and urge the need to place this topic in a broader context that connects energy production, related water consumption and environmental pollution of air and water (Kumar and Saroj, 2014). Besides the pollutants in air and water, also attention is needed for the pollution of the soil and thereby the crops that are grown on them (dos Santos-Araujo and Alleoni, 2016). In general, the major forms of pollution are contamination (occurs when chemicals are released by spill or underground leakage), water pollution (by the discharge of wastewater from commercial and industrial waste into surface waters) and air pollution (the release of chemicals and particulates into the atmosphere). All these types of pollution are also indirectly related to contaminated foods, which in turn bring an extra risk for the consumers.

1.2. Soil contamination

Soil contamination is caused by the presence of man-made chemicals in the natural soil environment and is typically caused by improper disposal of waste, agricultural chemicals, or industrial activity. Contamination is correlated with the degree of industrialization and intensity of chemical usage, and frequently consist of heavy metals (such as lead), petroleum hydrocarbons, polynuclear aromatic hydrocarbons (such as naphthalene and benzo(a)pyrene), solvents, and pesticides (George, Joy *et al.*, 2014). As the seriousness of this issue is highly recognized, efforts to remediate organic pollution from soil are explored. Some applications are identified as promising tools (such as manufactured nanoparticles to remove organic pollutant from soil), but it is questioned whether the introduction of these new particles might lead to new environmental concerns in the future (Li, Chen *et al.*, 2016).

1.3. Water contamination

Only less than 0.01% of water present in our world is fresh water (Piccoli, Kligerman *et al.*, 2016), but since it is an essential factor to keep life as we know it possible, and thus clean fresh water is of the highest priority. Unfortunately, water pollution is daily causing deaths as clean drinking water is not accessible to all (Li, Chen *et al.*, 2016). In addition, polluted areas as for example found in China, have lakes and rivers which are not even suitable anymore to be cleaned to provide safe drinking water (Li, Chen *et al.*, 2016). In addition to the acute problems of water pollution in developing countries, developed countries also continue to struggle with pollution problems. The Sano River in Italy is probably the most polluted river in Europe. Its pollution is derived from the urban density, agricultural and industrial activities and consists of *a.o.* metals, boron, cyanides, chlorides, nitrates, fluorides and sulphates (Lofrano, Libralato *et al.*, 2015). Besides these man-made chemicals, also organic contaminants pollute fresh water sources. For example, algae blooms are frequently observed in fresh water, presumably intensified by global warming. The hazardous toxins that are produced by these cyanobacteria are difficult to remove from fresh water sources, which would be required in order to make it suitable for consumptions (Weller, 2013). In addition, wastewater has been linked to viral, bacterial and protozoan diseases leading to e.g. salmonellosis, shigellosis, cholera and hepatitis A (Dickin, Schuster-Wallace *et al.*, 2016). In the capital of Bangladesh, Dhaka, it was shown, however, that the use of improved water sources and sanitation had a significant positive impact on the incidence of childhood diarrhea (Kamal, Hasan *et al.*, 2015). Therefore, it is essential that, through human intervention, the water quality will significantly be improved.

1.4. Food contamination

Food contamination refers to the presence of harmful chemicals and microorganisms in food which can cause consumer illness. Both soil and water pollution influences the agricultural suitability of the available land. About 70% of water usage is covered by the agricultural sector, and wastewater is used more and more used for irrigation, with the potential risk for crop contamination. It is crucial to realize that contaminants are not only entering the crops planted on polluted soil, but also a large amount of these potentially polluted foods are converted into animal feeds, leading to adverse health effects also in cattle (Coufal-Majewski, Stanford *et al.*, 2016). It is therefore essential to balance the steps taken to reduce health risks with the increasing need for food security and sufficient nutrition (Dickin, Schuster-Wallace *et al.*, 2016).

1.5. Air pollution

Air pollution is the introduction of particulates, biological molecules, or other harmful materials into the earth's atmosphere causing diseases, and even death to humans. Furthermore, damage to other living organisms such as animals and food crops, or the natural or built environment are accounted for by air pollution. In general, a distinction is drawn between ambient air pollution (AAP) and household air pollution (HAP) (Pant, Guttikunda *et al.*, 2016). AAP often contains particulate matter (PM) 2.5, PM10, ozone (O_3), nitrogen dioxide (NO_2), and sulfur dioxide (SO_2) (Liu, Cai *et al.*, 2016; Zhang, Li *et al.*, 2016). Besides the typical air pollution, pollution-dependent haze is identified as a separate class that should be discriminated from fog or mist. As fog consists of 90% water, it is mainly affecting traffic conditions due to bad visibility. Pollution-dependent haze, on the other hand, may already occur with a humidity of 80% and will also contain PM2.5, PM10, O_3, NO_2, and SO_2 (Liu, Cai *et al.*, 2016; Zhang, Li *et al.*, 2016). NO_2 and SO_2 in haze can react with the water droplets, leading to nitric acid and sulfuric acid, respectively, to be observed as a yellow or orange grey color of the haze (Liu, Cai *et al.*, 2016). Besides different compositions of AAP, there are also differences between the composition of AAP and HAP (D'Amato, Vitale *et al.*, 2015; Jiang, Mei *et al.*, 2016). Although there are compositional overlaps by means of PM, O_3, SO_2, NO_2, CO and lead (Pb), often the concentration and duration of the exposure are different. Furthermore, indoor exposure also includes combustion of solid fuels indoors, tobacco smoking and poor ventilation (Jiang, Mei *et al.*, 2016). This poor ventilation can lead to a build-up of another indoor pollutant, house dust, which has been shown to affect people with lung diseases through its' microbial content (Dannemiller, Gent *et al.*, 2016).

2. Adverse effects of air pollutants on human health

A recent systematic review and meta-analysis (SRMA) identified 43 systematic review (SR) studies or meta-analyses (MA) in which the relation between the ambient air pollutants PM2.5, PM10, NO_2, SO_2, CO and O_3 with a diversity of adverse health outcomes were investigated (Sheehan, Lam *et al.*, 2016). This considerable amount of SR and MA shows that there is a major interest in these air pollutants, and the outcomes of the studies conducted all point into the same direction: air pollution is related to multiple adverse health outcomes. However, the composition of air pollution is diverse throughout the world, and the role of meteorological factors (including atmospheric pressure, temperature and humidity) (D'Amato, Vitale *et al.*, 2015; Wang, 2016) in aggravating the effects of pollution are still not fully clear. Also changing lifestyle habits like the transition from coal combustion to a mixed coal smoke and motor vehicle emission lead to altered air pollutant composition throughout the years (Liu, Cai *et al.*, 2016). Furthermore, different governments and organizations have put variable regulation limits on these pollutants to reduce the risks. The United States Environmental Protection Agency (EPA), the World Health

Organization (WHO), the European Commission (EC), the Chinese Ministry of Environmental Protection (MEP) and the Environmental Protecting Department (EPD) of Hong Kong have declared different standard limits for these pollutants (Yi, Lo *et al*., 2015). These discrepancies complicate the direct comparison of studies conducted in different geographical areas. Interestingly, studies comparing different situations within the same country are showing that urbanization is the leading cause of pollution-induced disease developments. For example, Zhang *et al*. have shown that there is now sufficient evidence to indicate that the observed detrimental impact of environmental pollution on asthma and allergic disease first observed in West China is now also occurring in East China (Zhang, Qiu *et al*., 2015).

Another interesting finding is that commercial airliners routinely "bleed" compressed air to the cabin that is extracted from the aircraft engines. This unfiltered air may sometimes be contaminated with hydraulic fluids or synthetic jet engine oils. Medical record reviews of exposed airline crewmembers showed acute respiratory and/or central nervous system symptoms, again emphasizing the need to learn more about which airborne pollutants affect human health (Abou-Donia, Abou-Donia *et al*., 2013; Reneman, Schagen *et al*., 2015). These studies show that a better understanding of when, where and how humans are exposed to airborne pollutions is essential to estimate its possible impact on human health.

2.1. Indirect health effects

Man-made pollutants like O_3 and NO_2 not only directly trigger disease development in humans, but they can also affect plants that are exposed to these pollutants. This exposure can impact pollen protein (Frank and Ernst, 2016) as well as the pollen-derived lipids (Traidl-Hoffmann, Kasche *et al*., 2003) leading to modified immune responses in humans. Of course, the timing and concentration of pollution-exposure to the plant during the different seasons is a key element in this indirect impact of pollen-allergenicity on humans. These studies bring the realization that pollution also makes plants more prone to protect themselves against the damage caused by pollutants. Unfortunately, the major proteins involved in this specific defense mechanism are often the leading cause of disease-priming in humans after ingestion or inhalation.

Similar research is performed within the fungal kingdom, albeit very limited, even though fungal spores can have equal or even more direct effects on human health (Bush and Prochnau, 2004; Gioulekas, Damialis *et al*., 2004). As a matter of fact, specific fungal taxa like *Alternaria*, *Aspergillus* and *Cladosporium*, have been found responsible for hospital admissions due to severe asthma attacks, noticeably with a higher prevalence among children and with symptoms sometimes manifested as acute respiratory failure (Dales, Cakmak *et al*., 2000; Bush and Prochnau, 2004). Hence, it has been highlighted that fungi comprise a neglected and underestimated source of respiratory allergy, especially if compared to pollen allergies (Crameri, Garbani *et al*., 2014)2014. Beggs has also reviewed the need for research on fungal spores; however, little has been done since then (Beggs, 2004). Consequently, the exact relationship between pollutants, fungi and human health is still poorly described. Recent bio-monitoring and experimental data suggest that fungi seem to respond to environmental stress, like increased air pollution and climate change, in a strong but slow manner (compared to plants) (Damialis, Mohammad *et al*., 2015; Damialis, Vokou *et al*., 2015). Many of the allergenic fungal species are saprotrophs, endophytes, or plant parasites (Carlile et al., 2007)(Carlile, Watkinson *et al*., 2001). This means that they are closely related with (symbiotic relationship) or dependent on (parasitic relationship) their host organisms, plants. There are indications that this plant-fungal symbiosis leads to simultaneous long-term alterations and life strategy changes (Damialis, Mohammad *et al*., 2015): fungi may be elongating their growth phase and delaying their sporulation stage, whereas plants may be increasing the amount of pollen produced. In either case, more frequent or more severe respiratory allergy symptoms can be induced. Hence, Heinzerling *et al*. have shown that many allergens previously regarded as untypical for some regions in Europe have been underestimated, among which several fungal taxa (Heinzerling, Burbach *et al*., 2009). Particularly *Cladosporium* species, frequently observed within the most abundant spore concentrations in the atmosphere worldwide, seems to pose a forthcoming threat in allergic patients (Damialis, Mohammad *et al*., 2015).

2.2. Public health effects

The public concern around air pollution is increasing significantly due to the serious hazards to health; heart disease, chronic obstructive pulmonary disease (COPD), stroke and lung cancer are highly related to air pollution (Yi, Lo *et al*., 2015; Liu, Cai *et al*., 2016; Pant, Guttikunda *et al*., 2016). Furthermore, China's largest cities have a marked increase in the incidence of bronchial asthma (Liu, Cai *et al*., 2016; Wang, 2016). The awareness of the seriousness of respiratory disease development is also recognized in the establishment of the Global Alliance against Chronic Respiratory Diseases (GARD) by the World Health Organization in 2006 (WHO, 2015). Air pollution plays a well-documented role in asthma attacks, however, the role air pollution plays in initiating asthma is still under investigation and may involve a very complex set of interactions between indoor and outdoor environmental conditions and genetic susceptibility. Asthma is a complex respiratory condition operationally defined as a respiratory disease with three primary features (Leikauf, 2002). These include a) airway inflammation associated with cytokine formation, eosinophilic infiltration, and altered T-cell lymphocytic function; b) altered epithelial function associated with thickening of the basement membrane, mucin hypersecretion, and lost or altered cilia structure; and c) recurrent airflow obstruction often presenting in acute phases as decreased forced expiratory volume and reversible bronchospasm followed by persistent airway hyperreactivity. Although the frequency of asthma is higher among atopic individuals, not all people with asthma exhibit specific antigen–antibody responses (Leikauf, 2002).

Special attention is given to children and elderly, who are at higher risk to experience more severe adverse effects of air pollution (Zhang, Qiu *et al.*, 2015; Zhang, Li *et al.*, 2016). Children were shown to be more susceptible than adults, as they spend more time outdoors, have a higher activity level and minute volume per unit body weight, which leads to higher deposited concentrations of PM dose per lung surface. Another study showed that children between 6 and 10 years old had less nasal deposition of fine particles during light exercise compared to adults, suggesting that limiting exertion in children may be especially important for reducing their exposure to PM (Laumbach, Meng *et al.*, 2015). Elderly are regarded as more at risk due to the general gradual decline of their physiological processes over time. These conditions have often already led to pre-existing cardio-vascular and respiratory sensitivity which may further increase the susceptibility to PM (Zhang, Li *et al.*, 2016). In addition, multiple studies confirmed the association of exposure to ambient air pollution during pregnancy with adverse pregnancy outcomes (Poursafa, Baradaran-Mahdavi *et al.*, 2016; Qian, Liang *et al.*, 2016). Sbihi *et al.* showed that within-city air pollution exposure increased the odds of new asthma onset up to 25% in children of mothers living near highways during pregnancy (Sbihi, Tamburic *et al.*, 2016). This is in line with the strong consistent association observed between the distance to the nearest main road and allergic disease outcomes. Children living closer than 50 meters to a busy street had a higher probability of getting allergic symptoms, compared to children living further away (Parker, Akinbami *et al.*, 2009). In fact, one recent Los Angeles study found that eight percent of childhood asthma cases could be associated to living close (within 250 feet) to major roadways. A recent study in atopic volunteers showed that inhalation of diesel exhaust at environmentally relevant concentrations augments allergen-induced allergic inflammation in the lower airways (Carlsten, Blomberg *et al.*, 2016). In contrast to the adverse pregnancy outcomes when exposed to PM2.5, Capobussi *et al.* showed that exposure to SO_2 and CO seemed to postpone delivery, thereby making up for the maternal hypoxemic-hypoxic damage (Capobussi, Tettamanti *et al.*, 2016). Taken together, these studies suggest that pregnant women, young children and elderly are the populations that are most affected by the consequences of pollution exposure. Therefore, better care and protection from exposure of these risk populations will be of great value for future public health.

2.3. Health effects of exposure to specific air pollutants

To inform the public about the daily air quality, the EPA records the local air quality through its Air Quality Index. This AQI shows the levels of five major air pollutants, as they have been implicated to have great impact on human health (Gardiner, 2011).

The first two major pollutants are comprised of two size categories of Particulate Matter (PM). PM with a diameter between 2.5 and 10 μm are also referred to as PM10 or coarse particles. These particles can penetrate the thoracic airways and are often derived from soil and other crustal materials (Liu, Cai *et al.*, 2016). Particulate Matter with a diameter between 0.1 and 2.5 μm are referred to as PM2.5 or fine particles, and are primarily derived from secondary sulphate/nitrate, coal combustion, traffic emissions, dust/soil, secondary organic aerosol and industry (Zhang, Qiu *et al.*, 2015). They contain primary pollutants (e.g. gases originating from combustion processes) and secondary pollutants (e.g. by reactions of these primary pollutants with other components in the atmosphere) (Liu, Cai *et al.*, 2016). The proportion of PM2.5 in the distal pulmonary tissues was found to be three times larger than that of PM10 (Zhang, Li *et al.*, 2016). Around 81 million Americans live in areas that fail to meet national air quality standards for particulate matter (Parker, Akinbami *et al.*, 2009; Gardiner, 2011). Multiple studies have reported specifically on the relation between PM-exposure and adverse health outcomes. Lamichhane *et al.* have performed a meta-analysis of the exposure to PM and adverse birth outcomes. They concluded that their meta-analysis supported the adverse impact of maternal exposure to PM during pregnancy on the birth outcome, but also indicated that the variation in effects by exposure period and sources of heterogeneity between studies is complicating a strong causal relationship (Lamichhane, Leem *et al.*, 2015). Large geographical differences in PM2.5 concentrations were found comparing North America versus Asia (12 $\mu g/m^3$ versus 38 $\mu g/m^3$ respectively), making direct comparisons of PM2.5-induced health issues difficult (Pant, Guttikunda *et al.*, 2016). In relation to this, an increase of 0.58% of the respiratory mortality for every additional 10 $\mu g/m^3$ PM10 and 8% more hospitalizations due to respiratory complaints with an increasing concentration of 10 $\mu g/m^3$ PM2.5 have been reported (Xing, Xu *et al.*, 2016). The percentage relative risk for hospitalizations due to total respiratory diseases increased mostly due to an increment of 10 $\mu g/m^3$ of the pollutant PM10, followed by SO_2, and O_3 (Freitas, Leon *et al.*, 2016). In addition, the majority of people in developing countries live in population-dense areas that do not meet local air-quality guidelines, whereas in Europe it is the other way around (Pant, Guttikunda *et al.*, 2016). Lu *et al.* aimed to provide an estimate of the magnitude of adverse health effects of PM10 and PM2.5 pollution in the Chinese population. They concluded that short exposures to PM10 and PM2.5 are associated with increased mortality, but evidence of constituent-associated health effects, long-term effects and morbidity in China is still inadequate (Lu, Xu *et al.*, 2015). In Canada and the United States, long-term exposure to PM2.5 increased the chances of both cardiopulmonary complaints and lung cancer mortality, as shown by an extension of the average life span with 0.35 years for every 10 $\mu g/m^3$ decrease of PM2.5 (Xing, Xu *et al.*, 2016). Besides the clinical evidence, many groups are focusing more on the mechanism by which PM affect the physiological processes. The results range from declined non-specific immune defense, less viable macrophages, a more pro-inflammatory status of immune cells, and a lower capacity of macrophages to phagocytose (Xing, Xu *et al.*, 2016).

The third major pollutant, NO_2 can both act as a reducing agent as well as an oxidizing agent that easily combines with water to form nitric acid. When this happens with airborne water, it results in acid rain. Nitric acid is also a common component of pollution-dependent haze (Liu, Cai *et al.*, 2016). A large European cohort study (ESCAPEs study) recently evaluated the impact of traffic pollution (studied as NO_2 and NOx) on the quality of life (QoL). Probably due to the bias related to susceptibility (e.g. avoidance), moderate exposure levels or confounders related to the type of residential area, there was no difference in the impact of air pollution on QoL between controls, asthmatics or individuals with chronic rhino-sinusitis (Sommar, Ek *et al.*, 2014). Another study performed in London children concluded that exposure to traffic pollution (containing NO_2, NO, NO_x and PM) may cause a small overall reduction in lung function and may increase the prevalence of children with clinically relevant lung function reduction (Barone-Adesi, Dent *et al.*, 2015). Like NO_2, the fourth major pollutant SO_2 is a molecule that can both act as a reducing agent as well as an oxidizing agent. It can therefore alter many different compounds, and subsequently has a major influence on the suitability of a habitat for its plants and animals (Liu, Cai *et al.*, 2016). Compared to NO_2 and SO_2, the fifth major pollutant ozone (O_3) is the most powerful oxidizing agent, and, in high concentrations, will damage respiratory tissues in animals and even plants (Liu, Cai *et al.*, 2016). In 2013, according to the American Lung Association, around 38% of the Americans lived in areas with unhealthful levels of ozone. It has been shown that long-term ozone exposure increased the risk of developing the Acute Respiratory Distress Syndrome (Parker, Akinbami *et al.*, 2009; Gardiner, 2011; Ware, Zhao *et al.*, 2016). In addition, patients with chronic obstructive pulmonary disease (COPD) are hospitalized more frequently when exposed to O_3, NO_2 and SO_2 levels $>10\ \mu g/m^3$ (Ghanbari Ghozikali, Heibati *et al.*, 2016). Multiple studies have further investigated the effects of O_3 on lung function, showing a significant drop in FEV1 and a positive association between O_3 and asthma emergency visits in children (Zhang, Qiu *et al.*, 2015).

These studies show that each pollutant affects different organs through a different mechanism. Therefore, the timing and sequential order at which an individual is exposed will determine the disease outcome. A better understanding of the interaction between pollutants and the window of opportunity to repair the affected tissue will help to design improved prevention and therapeutic approaches.

In addition to the role air pollutants play in triggering severe allergic reactions and asthma attacks, especially the combination of pollution and allergens such as pollen is gaining interest. Reviews on this subject showcased frequent instances of interactions between fragments of airborne pollen and atmospheric pollution: there is growing evidence supporting the fact that pollen allergens can interact with air pollutants by adhering to the surface of pollen grains or paucimicronic allergen-carrying particles, with air pollutants thus modifying the antigenic potency of these particles (e.g. (D'Amato, 2000)).

3. The Social-Economic burden of pollution-induced diseases

In 2008, 1.3 million deaths were reported due to air pollution (Jiang, Mei *et al.*, 2016). The WHO reported that in 2012 around 7 million people died as a result of air pollution exposure, of which 3.7 million deaths from urban and rural sources worldwide. Regionally, low- and middle-income countries in South-East Asia and Western Pacific Regions had the largest air pollution-related burden in 2012, with a total of 3.3 million deaths linked to indoor air pollution and 2.6 million deaths related to outdoor air pollution (WHO, 2014). The causes of death caused by outdoor air pollution can be divided into different diseases: ischaemic heart disease (40%), stroke (40%), chronic obstructive pulmonary disease (COPD, 11%), lung cancer (6%), and acute lower respiratory infections in children (3%) (WHO, 2014). He *et al.* found significant associations of PM2.5, PM10, NO_2 and SO_2 with daily 'years of life lost' (YLL) and daily death counts in Ningbo, China. Interestingly, the associations with both outcomes were more evident in the elderly (He, Yang *et al.*, 2016). These findings are in line with the earlier report of Guo *et al.* that showed the mortality risk was higher for older people than for those aged 65 years or younger. Interestingly, they also showed that the effect estimates of PM2.5 and PM10 on YLL were higher in women than men, with the opposite for SO_2 and NO_2 (Guo, Li *et al.*, 2013). Similar findings have been reported on the relation between air pollution and premature elderly deaths in Moscow, Russia (Revich and Shaposhnikov, 2010; Shaposhnikov, Revich *et al.*, 2014).

3.1. Social impact of air pollution

There is relatively little people can do about their daily exposure to (air) pollutants. There are advises that aim for proper water intake to improve the disposal of water-soluble pollutants, and there are indications that sufficient anti-oxidant intake (a.o. vitamins), fish oil supplements or high flavonol cocoa might help the human body to lower the damage by pollutants (Cai and He, 2016; Zhang, Li *et al.*, 2016). Laumbach *et al.* have reviewed the various non-nutritional individual-level strategies for reducing exposure risk, which all influence the socio-economic situation of an individual (Laumbach, Meng *et al.*, 2015). The identified strategies include the reduction of personal exposure to ambient air pollution by staying indoors, cleaning indoor air with portable or central air cleaning systems, reduced exercise, avoiding outdoor activities when and where air pollutant levels are higher, reducing exposure in microenvironments near sources such as traffic, and the use personal protective equipment (respirators) (Laumbach, Meng *et al.*, 2015). Multiple of these advices are also addressed elsewhere (Cai and He, 2016; Jiang, Mei *et al.*, 2016; Pant, Guttikunda *et al.*, 2016), and all impact the quality of life of people with respiratory diseases like asthma or COPD. Some advises are specifically aimed at parents: when walking outdoors, choose a route that avoids major streets or highways where possible. Take children to playgrounds that are not next to major highways. Further, take any steps to ensure that new schools and housing developments are not placed near busy roadways, ports, rail yards or other industrial areas where the risk of diesel exposure increases. In addition, people living in an area with very high air pollution are advised to consider installing air filters inside their home (Parker, Akinbami *et al*., 2009; Gardiner, 2011).

Besides the economic and emotional costs that are accompanying the above described adjustments to air pollution, exposure to air pollution and associated health effects are often interlinked with socio-economic status as well as socio-cultural norms of the individual (Neidell, 2004; Pant, Guttikunda *et al*., 2016). For example, it has been shown that lower median incomes have higher levels household exposure compared to households with higher median incomes possibly concomitant with the tendency to live in more crowded conditions, co-habitation with cigarette smokers, and higher indoor PM levels (Pant, Guttikunda *et al*., 2016). Studies that focus on the socio-economic relationship between health outcomes and pollution are often showing results on pregnancy and young infants. For example, Chan *et al*. developed a socio-economic status (SES) index specifically for Canada, allowing more precise examining of the health outcomes from environmental pollution. They corroborate with the current literature: increased rates of preterm births, low birth weight and small for gestational age are correlated with a lower SES in case of PM2.5 exposure (Chan, Serrano *et al*., 2015). Similar findings have been reported in North Carolina, USA; a stable but negative association between air pollution exposure and adverse birth outcomes, with a further increased risk in the more socially disadvantaged populations (Gray, Edwards *et al*., 2014). Kathuria and Khan (2007) have also commented on the inequity in air pollution exposure in the Indian context. Not surprisingly, the relationship between socio-economic conditions and pollution exposure is expected to vary across communities and countries as also shown by Yap *et al*. They showed that in lower-SES South Coast areas, PM2.5-associated hospital admission rates for all respiratory outcomes were predominantly positive whereas results in the Central Valley were variable, often tending toward the null. These distinct patterns could be attributed to the heterogeneity of regional confounders as well as the seasonal variation of emission sources of PM2.5 (Yap, Gilbreath *et al*., 2013).

As described above, especially elderly experience premature death due to air pollution. As China has become an aging society, and is troubled by significant air pollution, research specifically aimed to analyze the effect of air pollution and rural-urban difference on mental health of the elderly in China was conducted. They showed that around 28% of the elderly people had psychological disorders. Air pollution significantly influenced the mental health of the elderly. In China, the urban elderly had a better psychological status than the rural elderly. The female elderly had more serious mental health problems. Marriage, education, and social activities had positive effects on the mental health of the elderly (Tian, Chen *et al*., 2015). However, this association of air pollution and depressed mood could not be confirmed in individuals from four European cohorts (Zijlema, Wolf *et al*., 2016). Morbidity and mortality from asthma are high in older adults and quality of life (QOL) might be lower, although standardized measurements of QOL have not been validated in this population. Traffic pollution exposure was the strongest predictor of poorer asthma-related QOL in older adults with asthma (Kannan, Bernstein *et al*., 2015).

3.2. Economic impact of air pollution

In 2000, the total losses due to O_3-induced crop damage in Spain accounted 20.7 M□, which are reduced to 18.8 M□ in 2020. The bulk of reduced economic loss concentrates on wheat, potato and grapes (Vedrenne, Borge *et al*., 2015). In the United States, the impact of O_3-induced crop damage was observed for maize and soybean from 1980 to 2011. They showed that over that period production of rain-fed fields of soybean and maize were reduced by roughly 5% and 10%, respectively, costing approximately 9 billion USD annually (McGrath, Betzelberger *et al*., 2015).

Besides the economic losses through crops, a large economic burden because of air pollution is found in the health care system. In 2014, asthma affected 334 million people worldwide. In Asia, it is more pronounced in South-east Asia and the Western Pacific regions where there is an estimated 107 million sufferers (Price, David-Wang *et al*., 2016). About 25 million Americans are intimately acquainted with the symptoms of an asthma attack (Gardiner, 2011). During an asthma strike, the airways become constricted, swollen, and are filled with mucus. The chest feels tight, causing cough or wheezing. In severe cases, asthma attacks can be deadly, as they are for more than 3,000 people every year in the United States (Gardiner, 2011; Roy, Sheffield *et al*., 2011). According to the Centers for Disease Control, asthma keeps children out of school for a total of more than 10 million lost school days each year and sidelines them from physical activity. Later in life, employers lose 14 million work days every year when asthma keeps adults out of the workplace. The disease is also responsible for nearly 2 million emergency room visits a year (Parker, Akinbami *et al*., 2009). In recent years, it has been shown that air pollution from cars, factories and power plants are a major cause of asthma attacks, affecting over 131 million Americans. Roughly 30 percent of childhood asthma within the USA is due to environmental exposures, with an associated cost of 2 billion USD per year (Roy, Sheffield *et al*., 2011). A Spanish study showed that a more strict regulation of the air quality resulted in a decline of the number of years lost due to PM2.5 air pollution from 230,700 in 2002, towards a predicted level of approximately 195,500 years until 2020 (Vedrenne, Borge *et al*., 2015). In addition, an Estonian analysis showed that air pollution results in 3859 Years of Life Lost (YLL) per year. When dividing the YLL by the number of premature deaths, the decrease in life expectancy among the actual cases is around 13 years. As for the morbidity, the short-term effects of air pollution were estimated to result in an additional 71 respiratory and 204 cardiovascular hospitalizations per year. The biggest external costs are related to the long-term effects on mortality: this is on average 150 M□ annually. In comparison, the costs of short-term air-pollution driven hospitalizations are only 0.3 M□ (Orru, Teinemaa *et al.*, 2009).

As mentioned above, there is a clear link between PM2.5 exposure during pregnancy and preterm birth. It has been shown that in 2010, around 15,808 preterm births within the USA could be attributed to PM2.5 exposure. The concomitant preterm birth cost was estimated at 4 billion USD, of which 760 million USD were spent on medical care (Trasande, Malecha *et al.*, 2016). Another study in South Carolina estimated the incremental costs of comorbidities observed in preterm infants to range from 4.529 to 23.121 USD. Whenever surgery was necessary, incremental costs could get as high as 41.161 USD. Incremental comorbidity costs are additive, so the costs for infants with multiple comorbidities could easily exceed the high of 41.161 USD (Black, Hulsey *et al.*, 2015).

Taken together, medical care, loss of school and workdays, and crop waste due to pollution all have a major economic impact. Improvements of the air quality is therefore of great importance for many governmental bodies and constant monitoring is implied as an essential step in this step. To better assess the severity of air pollution at a wider range of locations, new devices have been developed. An example is the use of a Static Sensor Network (SSN), in which the sensor nodes are typically mounted on streetlights, traffic light poles, or walls (Yi, Lo *et al.*, 2015). In a Community Sensor Network (CSN), the sensor nodes are typically carried by users, and in a Vehicle Sensor Network (VSN), the sensor nodes are typically carried by buses or taxis (Yi, Lo *et al.*, 2015). By utilizing and further developing these advanced sensing technologies, air pollution can be monitored with higher precision, which might lead to better solutions for the protection of the public health (Yi, Lo *et al.*, 2015).

4. Conclusion

By 2050, 66% of the world's population will be urban. The subsequent major forms of pollution of this urbanization are soil-, water-, and air pollution, and as a consequence polluted foods and feeds. This implicates that on a daily basis, humans are exposed to a multitude of pollutants, that each, on its own specific way, affect human health. In general, pollutants affect different organs, leading to multiple diseases such as heart disease, pulmonary disease, cancer, and fatal respiratory infections. Besides the major impact of the onset of these diseases in early life, also the effect of pollution during pregnancy is linked to adverse birth outcomes. After the onset of disease, especially young children and elderly are experiencing more severe complaints due to pollution exposure, leading to a strong reduction of the Quality of Life. Subsequent direct and indirect socio-economic costs are negatively impacted by a lower socio-economic status of the individual. Studies comparing the health situation before and after the implementation of air quality measures by governmental bodies have shown that a better air quality is related to lower crop wastes and improvements of the Quality of Life and lower Years of Life Losses. Therefore, air pollution should be considered as a modifiable risk factor in the prevention of non-communicable diseases like asthma. However, additional research is needed to improve our understanding of how the different air pollutants influence human health, and whether improved lifestyle factors like nutrition, living conditions and medical expertise can help individuals to reduce the negative health effects caused by pollution.

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