Mar 17

# The effects of anthropogenic outdoor air pollution on human health

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A summary report

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## *EXECUTIVE SUMMARY*

*The World Health Organisation (WHO) has said that the dangers posed by air pollution are far greater than previously though, is described as "one of the greatest hazards to human health" and as such has been declared a global health emergency. The evidence assembled in this document supports that assertion.*

*The overall research consensus is that since early last century there has been an increase in mortality and morbidity from short-term exposure to various airborne pollutants (such as particulates, $NO_2$, $SO_2$, CO and $O_3$). Also, in the last 10-15 years (in line with changes in technology and fuels), the impact of long-term exposure has been more significant than originally thought.*

*There are consistent results relating to the effects on life expectancy, cardiovascular health and lung cancers.*

*Life Expectancy: The results of many studies globally have shown that exposure shortens life expectancy. Outdoor air pollution is said to cause 50,000 deaths a year in the UK – and this figure continues to grow.*

*Cardiovascular health: Well-documented and significant impacts are identified (especially long term effects), as well as highly persuasive results relating to the incidence of strokes. A moderate increase in small particulates can lead to an increase of 12% in cardiovascular related deaths.*

*Lung cancer: It is proven that pollutants can be carcinogenic and entire populations are being put at undeniable risk. In Europe it has been proven that a moderate increase in small particulates can increase the risk of lung cancer by up to 22%.*

*In addition to these three well-researched impacts, there is a growing body of evidence relating to the effect of air pollutants on the respiratory system, foetal development and neurodevelopment and degeneration. Examinations of neuro-function, neurodevelopment and neurodegeneration have linked air pollution with cognitive function defects (ADHD, memory loss, reduction in IQ), behaviour deficits (reduced attention and productivity) and neuro-inflammations. Of increasing concern and importance lies the effect of air pollutants on children. Research into these effects is on the rise, with convincing studies proving alterations in young respiratory systems during growth years, and more recent findings in the impacts on their mental and genetic health, much of which can start as early as in the womb.*

*The conclusion is clear - the risk posed to human health from anthropogenic air pollution is significant, undeniable and will prove to be a real challenge for this and future generations. There is a critical need for further data and research, as well as dealing with the problem itself - unlike many other health threats, entire populations are at risk, and for many of the known pollutants, there is no safe level of exposure.*

# 1. Introduction

## 1.1 Purpose of the report

> According to the World Health Organisation (WHO) the dangers posed by air pollution are far greater than previously thought and is described as one of "the greatest hazards to human health"[1].

The purpose of this report is to provide an up-to-date review of all of the research and publications on anthropogenic outdoor air pollution and its effect on human health. This research shall come from all sources, including peer-reviewed literature, NGO publications and media articles – with the most relying results coming from meta-analyses of multiple studies and large research projects conducted over a number of years. The aim is to firstly see whether similar conclusions are reached throughout the range of sources, or whether discrepancies arise, and to secondly identify gaps in the research.

Before the literature review begins, it is important to detail the types of air pollution that have been studied and their sources, as some publications do not specify individual pollutants but air pollution as a whole. After this, there shall also be a short review of the overall effects of air pollution, as well as a discussion on the research designs of the studies included. The reason for this is that it is essential to understand the strengths and weaknesses of the investigation methods themselves before attempting to examine the conclusions reached.

## 1.2 Opening Statement

It is commonly understood that pollution is a by-product of all economic and societal activities[2]. For much of recent history anthropogenic air pollution has been a product of coal fires, power plants and heavy industry. Increasingly in today's society, with improvements in process technologies, clean fuels, filtration of gases and the export of most polluting industries to countries with lower wages and less pollution controls, as well as the emergence of new sources such as motor vehicle transport[3] from petrol to diesel, pollution has a new face. Modern pollution is now less visible, meaning that understanding and communicating the risks is now even more of a challenge[4].

With a steady rise in actionable data around air pollution and rapidly advancing technologies and 3D modelling, scientists are identifying newer, and mostly smaller toxic particles and systems. This has allowed scientific short and long-term research projects to advance and carry out studies to detect how, and to what extent, these harmful elements interact with the human body[5].

# 2. Air Pollution Explained

## 2.1 Types and sources of air pollution

As stated above, human activities are the main source of air pollution, but the pollutants can also have natural sources such as forest fires and volcanic activity. For the sake of this report, the focus shall remain on anthropogenic outdoor air pollution, the different types and sources described in the table below [6] [7].

These pollutants are categorised into two groups:

- Primary pollutants – which come from human processes
- Secondary pollutants – result from the interaction of primary pollutants with the atmosphere

| Primary pollutants | Source |
|---|---|
| Sulphur oxides (SOx)/sulphur dioxide ($SO_2$) | Combustion of fuels containing sulphur, mostly coal and oil, produced during metal smelting and other industrial processes |
| Nitrogen oxides (NOx) /nitrogen dioxide ($NO_2$) | Cars, trucks, electric power plants and other industrial processes |
| Carbon monoxide (CO) | From combustion processes low in oxygen, main source is motor vehicles, but also from burning wood, industrial processes and non-transportation fuel combustion |
| Carbon dioxide ($CO_2$) | From combustion processes, cars and power plants |
| Particulate Matter<br>• $PM_{10}$<br>• $PM_{2.5}$<br>• $PM_1$ | Larger "coarse" particles ($PM_{10}$) come largely from windblown dust, vehicles travelling on unpaved roads, and crushing and grinding operations.<br>"Fine" particles known as "$PM_{2.5}$" of 2.5 micrometers to 1 micrometer in diameter- produced by motor vehicles, coal-burning electric power plants, factories as well as from residential fireplaces and wood stoves.<br>$PM_1$: of 1 micron or less in diameter. More research is needed on $PM_1$, understanding their source and effect are in the early stages of development. |
| Ammonia | Used to fertilise crops and emitted from agricultural processes and farm animals |
| Volatile organic compound | Evaporates from sources such as vehicle exhausts, cleaning agents, furniture polish and fabric softeners |

| | |
|---|---|
| Lead | Produced by lead smelters, metal processing, contained in old paints and plumbing |
| Persistent organic pollutants (POPs) | Produced through industrial processes and waste incineration |
| EPFRs - Environmentally persistent free radicals | Formed within particulate matter, emitted from cars, cooking stoves, factories, waste incinerators, wood fires, tobacco smoke. |
| polycyclic aromatic hydrocarbon (PAH) | Found in vehicle emissions, oil and coal burning, agricultural burning, tobacco smoke |
| Secondary pollutants | Source |
| Particulate matter (from sulphates and nitrates) | Particles which are either man made or natural (such as sulphates and nitrates) interact with other compounds in the air to form fine particular matter. These tiny bits of soot can travel hundreds of miles downwind of the original pollution sources |
| Ozone | Formed from a chemical reaction of ultraviolet (UV) radiation and oxygen, dissociating their molecules into separate oxygen atoms during sunlight |

Many publications have discussed specific health effects associated to overall air pollution. As the table above outlines, there are many pollutants capable of causing harm, yet their type and abundance in environments vary. Therefore, readers will need to take into account the social and economic influences of the area to detect which particles a study may be referring to, when being confronted with general ‘air pollution’. For example, those areas where there is high levels of primary industry will have a very different pollution profile to those areas where vehicle emissions are the main source.

## 2.2 Effects of air pollution

As referred to before, the focus of this review shall be on the direct effects on human health from anthropogenic air pollution. However, air pollution does not just cause effects on human health, it can be detrimental or harmful to comfort, recreation, living conditions, personal welfare and economic growth, cause injury or damage to real or personal property, or interfere with the conduct of industry, commerce or transport[8]. Below is a complete list of these other effects of air pollution[9], which can be indirectly linked to health risks:

- Climate forcing
- Decrease in atmospheric visibility
- Acidification which can lead to a loss of flora and fauna
- Eutrophication and a decrease in biodiversity
- Damage to crops, forests, plants because of ground level ozone
- Impacts of heavy metals and organic pollution, which can lead to environmental toxicity and bioaccumulation
- Damage to materials and cultural heritage because of soiling, acidic pollution and ozone

> Toxins from eutrophication can damage the nervous, digestive, respiratory and cutaneous systems, as well as cause fatigue, headache, diarrhoea, vomiting, sore throat, fever and skin irritations.

# 3. Research Design

## 3.1 Research design

When measuring the effects of air pollution on human health there are two methods to do so: experimental and epidemiological. Both of these methods have their strengths and weaknesses and it is essential to recognise the potential determinants of these differences when comparing conclusions[10]. Also, it is important to state that collating and comparing studies of the same type in itself is also difficult as measurement techniques and definitions have changed over time[11].

Experimental studies expose people, animals, cell cultures or bio-material to well specified pollutants under controlled conditions with the risk of bias and confounding factors being reduced where possible. However, these studies can only focus on one or two pollutants at a time, and the real life situation is a lot more complex with greater degrees of uncertainty[12 13]. Such study subjects can be problematic as firstly, studies from animals cannot be generalised to humans and secondly the study of healthy adults cannot be generalised for the unborn, infants, adolescents or people with severe diseases. Finally it is difficult to look at long-term exposure effects as exposure to other toxic particles and further external environmental influences is difficult to avoid[14].

Epidemiological studies are conducted in the general population and selected groups where the effects can be studied over a broad range of outcomes including acute, subacute and chronic. The main issue with this however, is that none of the ailments relating to air pollution are air pollution specific and short term variations in air pollution are not the only cause of daily fluctuations in health problems[15]. Also, the complex way in which pollutants react together means that it can be very difficult or even impossible to trace the true cause of a health impact with certainty[16] and it is this air pollution exposure assessment and exposure misclassification which remains the most important source of bias in health effect studies[17]. Lastly, it is of grave importance to note that there may be ecological bias in some studies, especially epidemiological ones, because a simple summary measure could be too simplistic to provide a summary of a spatially variable pollution surface[18].

As stated previously, measurement techniques are constantly changing. In a first study of its kind, a 2016 project measured population activity patterns representing several million people to evaluate population-weighted exposure to air pollution on a city-wide scale. Mobile and wireless devices yielded information about when and where people were present; therefore collective activity patterns were determined using counts of connections to the cellular network. Evaluating population exposure to air pollution using spatiotemporal population mobility patterns warrants consideration in future environmental epidemiological studies linking air quality and human health[19]. This is further proof that we constantly need to be considering measurement techniques when comparing studies and research.

In summary, for both experimental and epidemiological investigations there is potential for publication bias. It has been estimated that the association between air pollution and various

health outcomes may be reduced by as much as 40% after adjusting for this publication bias[20]. In recent years the topic of air pollution and its impacts on the human body has gained evermore interest and attention and it is interesting to note that throughout the formation of this paper, studies with evidence of significant positive associations between air pollution and health effects are more likely to be published than negative papers.

# 4. Health Impacts

## Overview

Studies linking poor health and air pollution since early last century have seen a marked increase in mortality and morbidity following short-term episodes of high levels of air pollution[21]. As well as this, in the last 10 to 15 years it has become apparent that the long-term health impacts of less visible pollution are much more significant than originally thought[22]. This lead to the adoption of an ambient air quality level to safeguard the public[23].

Overall, air pollution has both acute and chronic effects on human health, affecting a number of different systems and organs[24] and below is an edited list of health outcomes where there is at least some evidence of an association with air pollution[25].

Acute effects

- Daily mortality
- Respiratory hospitals admissions
- Cardiovascular hospital admissions
- Emergency room visits for respiratory, asthmatic and cardiac problems
- Primary care visits for respiratory, asthmatic and cardiac problems
- Days of restricted activity
- Work absence
- School days missed
- Self-motivation
- Avoidance behaviour
- Acute symptoms
- Physiological changes

Chronic effects

- Mortality from chronic cardio-respiratory disease
- Chronic respiratory disease incidence and prevalence (asthma, chronic obstructive pulmonary disease)
- Chronic change in physical function
- Lung cancer
- Chronic cardiovascular disease

Other effects

- Low birth weight
- Pre-term delivery
- Cognitive development in infants

Now the basis of this report has been established, the next portion shall be looking at the specific health effects of exposure and what research and conclusions have been drawn globally. These health effects shall be categorised by short-term and long-term effects. The latter shall be split into:

Overall:

- Mortality and life expectancy
- Respiratory health (asthma and allergies),

- Lung cancers
- Cardiovascular health (cardiovascular disease and stroke),
- Diabetes
- Neurofunction (neuro-development changes and degeneration)

Children specific:

- Neurochanges (developing brain and autism)
- Diabetes
- Foetal growth
- Children growth years and developing organs

Emerging research areas

- Human genome system

## 4.1 Short-term effects

The British Lung Foundation states that because most pollutants are irritating to the airwaves, the short term effects of an elevated level of air pollution can include a cough or shortness of breath. This is especially true for people who have lung diseases such as asthma and chronic obstructive pulmonary disease (COPD), and those vulnerable members of society such as elder generations[26]. In addition, short-term effects can include illnesses such as pneumonia or bronchitis, discomfort such as irritation to the nose, throat, eyes, or skin or even headaches, dizziness, and nausea[27]. These effects in themselves can lead to an increase in hospitalisations, decrease in productivity and an increase in sick days. Further information on the short-term effects on cardiovascular health can be found in section 5, page 23.

A meta-analysis of previous studies released in 2012 also concluded that short-term exposure (for up to 7 days) to all major air pollutants (except ozone) is significantly associated with an increased risk of heart attack[28]. Furthermore, a meta-analysis of 33 epidemiological studies in China found an increase of 10 μg/m³ in $PM_{2.5}$ resulted in an increase of 0.38% in total mortality, 0.51% in respiratory mortality and 0.44% in cardiovascular mortality[29].

> One such study in Montreal, Quebec, in 2013 concluded that those individuals with certain health conditions, especially with diabetes and cardiovascular disease, hypertension, atrial fibrillation and cancer may be more susceptible to the short-term effects of air pollution[30].

Publication example/s

On the other hand, a 2017 study[31] into the relationship between short-term changes in ambient pollution ($PM_{2.5}$ and $O_3$) and the risk of recurrent ischemic stroke found no evidence of associations between previous-day air pollution levels and recurrent ischemic stroke. Research on the influence of air pollutants on risk of stroke recurrence is still in its infancy, and more research is necessary in studies that are adequately powered to understand the relation.

***While there is a chance of serious illness from short-term exposure to pollutants – the probability is relatively low, especially compared to the long-term implications discussed later. What is significant however is the 'low level' irritation discussed. These small changes will have a big effect on productivity and general wellbeing during people's everyday lives – which is particularly true for those who live and work in urban areas, meaning high economic impact and affecting the overall standard of living.***

## 4.2 Mortality and life expectancy

Firstly it is important to state that the total number of deaths in a given population cannot be changed by reducing levels of air pollution: it can only be postponed/make people live longer[32]. Measuring mortality and death rates is the easiest health ailment to measure due to the accessibility and formal requirements of the records and the clear distinction. This has meant that there have been numerous papers and articles written detailing the benefits of cutting air pollution on life expectancy. The overall consensus being that air pollution exposure shortens life expectancy[33], even at very low levels of exposure[34].

The most up-to-date research by the World Health Organisation (WHO) calculated that in 2012 3.7 million deaths globally were attributable to ambient air pollution resulting in it being the 13th leading cause of death worldwide[35] and 92% of the global population live in places where air pollution exceeds WHO limits[36]. This is compared to 1.3 million published for 2008. The main reasons for this large increase are[37]:

1. Additional evidence of the health effects
2. Increase in non-communicable diseases
3. Inclusion of rural populations (not just urban)
4. Use of lower counterfactual

This figure is more than Malaria and HIV/Aids combined and is set double by 2050 – based on a 'business-as-usual' emission scenario. These deaths predominately come from Asia[38] with one study from China calculating that observed air pollution contributes to 1.6 million deaths a year – roughly 17% of all deaths or 1 in 6[39].

In Europe $PM_{2.5}$ is responsible for 380,000 premature deaths a year[40]. In the UK the Environmental Audit Committee said poor air quality reduces the life expectancy of everyone in the UK by an average of seven to eight months and up to 50,000 people a year die prematurely because of it.[41]

A further large nationwide study examining the effects of very long-term exposure (25+ years) suggested that exposure has long-term effects on mortality that persist decades after that exposure, and that historic air pollution exposures influences current estimates of associations between air pollution and mortality[42].

A bit more localised still - a paper released by Kings College London in 2015 concluded that approximately 9,500 people die prematurely in London every year from exposure. This figure is double previous estimates[43] because it was the first study to count the impact of nitrogen dioxide on health, not just particulate matter[44]. Also, figures from the Office for National Statistics (commissioned by the campaign group Clean Air in London) ranked air pollution as contributing to all four of the main causes of deaths in each London borough over the last 12 years[45].

*Specific studies from across the globe:*

> A study in the UK found that removing all anthropogenic $PM_{2.5}$ could save the national population approximately 36.5 million life years over the next 100 years with an associated increase in life expectancy from birth of 6 months[46]

> A study by Brunkekreef in 2010 states that PM exposure reduces life expectancy by one or more years[47]

> The Aphekom Project, which was a Health Impact Assessment in 25 European cities in 12 countries, found there to be a gain in life expectancy of 0-22 months (depending on the city and averaging 5.8 months) at 30 years if $PM_{2.5}$ concentrations didn't exceed WHO – Air Quality Guidelines (AQG) of 10 µg/m$^3$

> A 3 year study in New Zealand, using census data from 1996-1999 and estimates of exposure levels, found the odds of all-cause mortality in adults increased by 7% per 10 µg/m$^3$ in $PM_{10}$ exposure and 20% per 10 µg/m$^3$ [48]

**Publication example/s**

***The only conclusion that can be drawn from these published figures is that air pollution is truly an invisible threat, one that affects everybody unknowingly yet seriously, with new research showing that the most disadvantaged are most at risk. There is substantial public awareness into the health effects of various lifestyle choices, diseases etc. – but it would seem awareness of air pollution is severely lacking and with the growing literature – it would seem we are only just scratching the surface.***

## 4.3 Respiratory health

In 2013, the European Environmental Agency stated that excessive PM exposure is as a problem because it penetrates the sensitive parts of the respiratory system[49], which can cause a number of health problems including asthma attacks, bronchitis and pneumonia[50].

The European Aphekom Project, detailed previously, found a link between a decrease in daily ozone mean and an annual decrease in respiratory hospitalisations and postponed respiratory deaths in the population aged 15 or more. However the total amount is quite small, just in the hundreds, whereas compliance with WHO – AQG for $PM_{10}$ is said to avoid 8000 hospitalisations for cardiovascular and respiratory causes[51].

**Publication example/s**

### Asthma

According to the British Lung Foundation, it is still unclear whether air pollution may increase the risk of developing asthma and allergies, but it is general consensus that it can prompt attacks or worsen the condition[52] and this has been increasingly backed up by recent research publications[53].

This conclusion is supported by a multidisciplinary review based on literature in 2013, which stated that there "is an increase risk of developing exacerbations for asthmatic patients and triggering attacks upon exposure to ozone, nitrogen oxides, particulate matter, dust mites and mould." However, there is a difficulty in establishing the link between individual pollutants and asthma[54].

Furthermore, according to Asthma UK[55]:

*" Air pollution plays a part in causing asthma in children and adults, as well as being a trigger that can make people's asthma symptoms worse. Two thirds of people with asthma have told us that traffic fumes make it worse and one third say a reduction in air pollution would make the most difference to their lives"*

Asthma UK also stated that children who suffer from asthma and spend many hours outdoors during rush hours are particularly vulnerable due to faster breathing rates and lungs that are still developing[56]. For more information on the health effects associated with children – go to Chapter 5, page 31.

> The link between air pollution and increased asthma attacks was studied in the UK following two spells of 'very high' air pollution records: 12th - 14th March 2014 and 29th March - 3rd of April 2014[57]. Public Health England recorded hospital visits that took place during these two periods and published their results in the Journal of Environmental Research in January 2015[58].

The paper stated that during the first spell of high air pollution, an excess of 1,200 consultations for breathing difficulties were recorded, and 100 cases of severe asthma, and in the second this rose to over 2,300 recorded consultations and over 400 cases of severe asthma. The research proved that a rise in respiratory conditions from asthma (including wheezing and chest pains) were detected[59] and made clear that real-time air pollution surveillance monitoring systems are of great value during poor air quality episodes as it is key to understanding the impact of such pollutants on community health[60].

> A study in Delhi blamed observed PM levels for 6.0 million asthma attacks a year[61] but they did not specify whether the patients have developed asthma from the PM exposure, or were just suffering more attacks because of it.

**Publication example/s**

The conclusion is undeniable (a view held and published by the WHO) - there is a causal relationship between exposure to air pollutants and aggravation of asthma[62]. However, whether it causes the disorder in the first instance requires further study.

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### ALLERGIES

In March 2015 a report was presented by the 249th National Meeting & Exposition of the American Chemical Society (ACS)[63] that examined how traffic-related air pollutants (TRAP) could increase the strength of chemical modifications in allergenic proteins[64]. The team found that the pollutants showed chemical modifications by binding together to create a more potent allergen that would make human allergies more severe[65]. The internal protein modifications that take place when exposed to ozone and nitrogen dioxide have the ability to increase the prevalence of allergies worldwide.

A 2016 study by Bowette at al stated that while the evidence linking traffic-related air pollution (TRAP), allergic airway diseases and reduced lung function in children is established – evidence concerning adults is scarce and inconsistent. According to this research, even relatively low TRAP exposures lead to an increased risk of adverse respiratory and allergic outcomes in genetically susceptible individuals[66].

Overall, it is clear that air pollution has an effect on the respiratory system, from increasing asthmatic spells and other respiratory conditions to impacting the internal genetic structure of those who suffer from asthma. More research needs to be done on understanding whether

pollutants can cause asthma all together and the extent of pollutant impacts on adult age allergies, and compare the effects on those that are physically fit to those who may already have a low immune system and suffer from any illness, disease or allergies. Also to finally research the role of genetics in susceptibility.

## 4.4 Lung cancers (and other types)

According to WHO's International Agency for Research and Cancer, ambient air pollution is a classified carcinogen, causing lung cancer and initial research is showing links with urinary tract/bladder cancer as well[67] [68], and other cancer types discussed later.

2013 was a year where the risk of lung cancer from air pollution made international news including The Guardian[69], NBC News[70], Press TV[71], India Today[72] and Headlines & Global News[73] and the source of all this coverage was the ESCAPE (European Study of Cohorts for Air Pollution Effects) project that combined data from 17 cohort studies in 9 European countries and almost 313,000 study subjects. This project looked into the long-term exposure of nitrogen dioxide and PM ($_{2.5}$ and $_{10}$) making it the largest study into lung cancer in history[74].

This study initially reviewed the scientific literature up until May 2007, where they found evidence showing an association between air pollution and lung cancer risk, however there were limitations throughout these investigations. These included:

- Small size of the cohort studies,
- Poor retrospective exposure assessment,
- Absence of or limited information about potential confounders
- Mortality used as an outcome instead of lung cancer incidence rate

The ESCAPE project overcame all of these barriers to provide the most up-to-date and reliable information on the risk to lung cancer. They statistically allowed for confounding factors including smoking.

The results showed that during the average 13-year follow-up 2095 people developed lung cancer. An increase of 5 μg/m$^3$ of $PM_{2.5}$ increased the risk of lung cancer by 18%, an increase of 10 μg/m$^3$ of $PM_{10}$ increased the risk by 22%, but there was no link between nitrogen dioxides and lung cancer. They also found that there was no threshold of risk, meaning that there are potential effects at all levels of exposure.

From this study, more papers were published using it as a basis. One such example[75] begins by stating that the risk from air pollution isn't as great as smoking (WHO, 2004), where smoking causes 71% of lung cancer worldwide, whereas air pollution just 8%, but the difference is that everyone is exposed to air pollution. They also talk of the shift in frequency of lung cancer types (i.e. from squamous cell carcinoma to adenocarcinoma) and different frequency distributions to types of lung cancer through-out the world: showing the need for future assessments of association between air pollution and specific types of lung cancer.

As well as the published ESCAPE article, there was also a video interview with one of the authors[76]. In the interview we learn that cell type specifics is also important: the squamous cell carcinoma is typical in smokers, whereas the adenocarcinoma is typical in non-smokers, and it is the latter one that is rising. This means that the effects of air pollution can be separated from that of smoking, reducing the risk of it being a confounding variable.

Furthermore, a publication from the Drexel University School of Public Health in Philadelphia in 2015, conducted a random systematic review and meta-analysis using 20 studies that provided either a good level of information on estimated individual exposure levels to particular pollutants, or provided observed lung cancers from various parts of the world. The studies varied by measured level of exposure and exposure assessment technique but came to find that the meta-analyses results support the hypothesis that there is indeed a relation between lung cancer and exposure to air pollution from traffic related $NO_2$. The study results showed that 4% of lung cancer was associated with a 10 µg/m$^3$ increase in exposure to $NO_2$, but the geographic variability is large. For example, $NO_2$ exposure was associated with 2% of lung cancer in Europe, 7% in North America and 11% in Japan[77].

> A 3 year study in New Zealand found a strong relationship between air pollution and lung cancer mortality, even in a country with low levels of pollution[78]

> A Japanese study established a strong link between the two, especially among non-smokers compared to ex and current smokers[79]

> Another investigation detailed that for each 10 µg/m$^3$ increase in fine particles resulted in an 8% increase risk for lung cancer[80]

> A Danish study looked into the concentration of NOx (as an indicator of air pollution from traffic) and the associated risk of lung cancer. It allowed for smoking and found a 37% increase in incidence rate ratio per 100 µg/m$^3$ increase of nitrogen oxides. It also estimated 14% of lung cancer cases were attributable to air pollution[81].

**Publication example/s**

Moving on from lung cancer, a number of studies have used the ESCAPE project data to research other types of cancer. One such 2017 study[82] looked into the increased risk of kidney parenchyma cancer, using the data cohorts from 14 of the European cohorts. Previous to this study, several publications indicated weakly increased risk among occupational groups exposed to gasoline vapours, engine exhaust, polycyclic aromatic hydrocarbons and other air pollutants, although not consistently. This study wished to calculate summary hazard ratios (HRs) and the meta-analysis showed higher HRs in association with higher PM concentration, albeit never statistically significant. The study provides suggestive evidence that exposure to outdoor PM at the residence may be associated with higher risk for kidney parenchyma cancer; the results should be interpreted cautiously as associations may be due to chance.

Another example came from Pedersen et al[83], using data from 4 European cohorts from the ESCAPE project to look at the association with increased risk of liver cancer. It was identified as a gap in the research; the deleterious effects of tobacco smoke have been well documented – whereas the risk of air pollution is less studied. As in the previous study, all exposures were associated with elevated hazard ratios, but none of the associations reached statistical

significance. Again, this provides suggestive evidence for an increased risk of liver cancer, but further research is required.

**From the evidence above, the link between air pollution and lung cancer is without doubt. The ESCAPE project and Drexel University School of Public Health confirmed the statement by The International Agency for Research on Cancer classifying outdoor air pollution and particulate matter as carcinogenic[84]. The paper provided a reliable and thorough analysis that seems to be supported by investigations from different parts of the world. Thus, the basis conclusion seems definite, yet there are still areas and cancers which need to be researched, i.e. more specific types of lung cancers, kidney, liver, urinary tract and bladder.**

## 4.5 CARDIOVASCULAR HEALTH

### CARDIOVASCULAR DISEASE (CVD)

The impacts on cardiovascular disease (CVD) from exposure to various air pollutants is very important to understand, as it is the leading cause of morbidity and mortality in Western Countries[85]. $PM_{2.5}$ has already been identified by the scientific community as a health risk, with the AHA (American Heart Association) 2010 scientific statement describing $PM_{2.5}$ exposure as "a modifiable factor that contributed to cardiovascular morbidity and mortality"[86].

Thus far, epidemiological studies have demonstrated a consistent increase in risk for cardiovascular events in relation to both short and long term exposure to present day concentrations of ambient PM[87]. One of the most important points detailed in the BMJ was that there is no 'safe' level of exposure[88]. The adverse health effects detailed below can occur even within the parameters set out by the EU Directive 2008/50/EC[89].

To begin, a narrative review in 2013[90] linked PM concentrations to several clinical manifestations of CVD including:

- Heart attack
- Stroke
- Heart failure
- Heart rhythm problems
- Venous thromboembolism (includes deep vein thrombosis and pulmonary embolism)

This review also stated that the influence of air pollution on health is not limited to PM, other gaseous pollutants may play an independent role in CVD.

With CVD, the long and short-term exposure effects are different, and also tend to threaten different members of the population. Generally, long-term exposure is found to be a greater overall risk to CVD, but short-term it is more dangerous for vulnerable patients with pre-existing conditions such as diabetes and underlying coronary or pulmonary disease, as well as the elderly and even those in lower socio-economic populations[91] [92]. The evidence for this is described below.

Long-term effects: A follow up study from the American Cancer Society took data from 151 US cities and found that an increase in 10 $\mu g/m^3$ of $PM_{2.5}$ increased the risk of death from cardiovascular causes by 12% and is a risk for those with or without existing cardio-metabolic disorders[93]. Similar results were also found in LA, Sweden, Germany and Holland[94].

Short-term effects:

- The National Morbidity, Mortality and Air Pollution Study (NMMAPS) had 50 million study participants in 20 of the largest US cities. This investigation found that an increase of 20 $\mu g/m^3$ in $PM_{10}$ resulted in a 0.06% increase in daily mortality from cardiopulmonary disease[95]
- The APHEA-2 study of 43 million people in 29 European cities found an increase of 20 $\mu g/m^3$ in $PM_{10}$ equated to an increase of 1.5% in daily cardiovascular mortality[96]

> A time series study by Pope and Dockery found an increase in 10 μg/m³ in mean $PM_{2.5}$ (over a 24 hour stretch) gave between a 0.4-1.0% increase in the risk of cardiovascular mortality[97]

> A 2016 study in London found an association between short-term exposure to traffic related air pollution and cardiovascular hospitalisations. With a conclusion that a more extensive monitoring is required in urban centres to further clarify the association[98].

As well as the risk of mortality, there have also been links with morbidity including ischemic heart disease, arrhythmia and heart failure. For example:

> A Finish study looking at the effect of fine particulates on ischaemic heart disease patients found that regional and long-range transport, traffic and biomass combustion promoted systemic inflammation – a risk factor for CVDs[99].

***To conclude, the evidence demonstrates that the long-term effects are a lot more significant than the short-term and the vast majority of these studies are large enough to be able to draw reliable conclusions. However, the short-term effects should not be underestimated as scaling it up to population risk makes it significant[100]. In addition, even though this evidence seems strong and convincing, the underlying mechanisms behind these health effects have yet to be fully identified, showing the need for still further research[101].***

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## STROKE

As stated previously, stroke is a manifestation of CVD and it is also one of the most well documented effects of air pollution. Many studies have demonstrated a positive association between an increase in outdoor air pollution and stroke but these conclusions have been largely inconsistent[102], and it is the nature of these inconsistencies that shall now be determined.

The most recent systematic review[103] (2015) from Edinburgh University looked at the association between short term air pollution exposure and stroke related hospital admissions and deaths. In total, they analysed 103 observational studies that covered 28 countries worldwide. Pollutants included in the analysis were carbon monoxide, sulphur dioxide, nitrogen dioxide, ozone and particulate matter ($PM_{2.5}$ and $PM_{10}$)

Results showed an association between carbon monoxide (1.5% increased risk per 1 ppm[1]), sulphur dioxide (1.9% per 10 ppb) and nitrogen dioxide (1.4% per 10 ppb) and stroke related hospital admissions or death. The weakest association was found for ozone. Additionally, both $PM_{2.5}$ and $PM_{10}$ were associated with hospital admissions or deaths due to stroke, by 1.1% and 0.3% per 10 µg/$m^3$ increment respectively. The first day of air pollution exposure was found to have the strongest association.

Furthermore, the most common conclusion from many of the investigations is that long-term outdoor air exposure has an association with ischemic stroke and not haemorrhagic stroke:

> A seven year Japanese study calculated that the relative risk of dying from ischemic stroke from air pollution is between 3 and 6% depending on the pollutant[104].

> Another study looked at nine US cities and the link between PM and hospital admission for ischemic and hemorrhagic stroke. This study found that an increase in $PM_{10}$ was associated with an increase in 1.03% in admission in ischemic stroke incidents on the same day, and there were similar results for CO, $NO_2$ and $SO_2$. However, for hemorrhagic stroke there was no association observed[105.]

> Conversely, there are a small number of studies that suggest an association with haemorrhagic stroke, all of which were conducted in Asian countries. One of the reasons given for this difference in conclusions between studies is the high frequency of cerebrovascular disease and haemorrhagic stroke in these countries, therefore allowing the detection of the health effects[106].

**Publication example/s**

Another common feature of these investigations is the effect of climatic conditions on stroke:

> First, a Canadian investigation[107] looked at nearly 6000 medical charts between 2003-2009 and the short-term effects of ambient air pollutants (PM, CO, $SO_2$, $NO_2$, $O_3$) on stroke. In addition they also used the relative humidity and temperature for analysis. They found a positive association between ischemic stroke and air pollution during 'warm' seasons, but no associations were evident with the other stroke subtypes (including haemorrhagic). Their findings also suggested that patients with a history of stroke, heart disease and diabetes were more vulnerable, just as stated previously

> A Taiwanese investigation found that on warm days, there was a significant positive association between levels of $PM_{10}$, $NO_2$, $SO_2$, CO and $O_3$, and both primary infracerebral haemorrhagic stroke and ischemic stroke admissions. However, on a cool day, only CO levels and ischemic stroke were significantly associated[108]

> A study combining US databases including the US Environmental Protection Agency Pollution Levels found statistically significant independent exacerbating effects of warmer, drier

[1] Units explained – ppm (parts per million) and ppb (parts per billion) are concentrations of the amount of one material in a larger amount of another material. µg/$m^3$ is the concentration of an air pollutant in micrograms per cubic meter of air.

air, upper respiratory infections, grass pollen, $SO_2$ and PM. This model supports the theory linking pulmonary inflammation to stroke[109]

**Publication example/s**

Another area of study is into whether long-term exposure to ambient air pollution can cause structural changes in the human brain.

> The Cardiovascular Epidemiology Research Unit at the Beth Israel Deaconess Medical Centre in 2014[110 111] drew on the topic of 'silent' strokes, which is caused by covert brain infarcts[112]. The stroke comes as a result of blockage in blood vessels that supply the brain. Understanding the causes of silent strokes is important as they increase the risk of overt strokes and thus developing dementia, depression and walking difficulties[113]. The study found that an increase in $PM_{2.5}$ was associated with 1.46 higher odds of covert brain infarcts[114], meaning that those living in more polluted areas have 46% higher risk of silent strokes[115].

> A follow-up study in Denmark looking at the increased risk of brain tumours from TRAP exposure didn't support the relatively strong linear association which was found in their initial study. The conclusion was that further research is required[116].

**Publication example/s**

The last point to be made is the association a few papers have drawn between air pollution, stroke and gender:

> An epidemiological study of nearly 25,000 people in China[117] during 2009 that found a significant association between $PM_{10}$ and $SO_2$ levels and stroke prevalence, but these associations were only significant in men.

> A small area ecological study[118] based on 113,465 census enumeration districts across England and Wales found that stroke mortality was 7% higher in men living 200m of a main road, compared to men living more than 1000m away. For women however, it was just 4%. This equated to 990 stroke deaths per year would have been attributable to road traffic pollution.

**Publication example/s**

**To conclude, the evidence of an association between pollution and subsequent stroke is persuasive and highlights the need to reduce exposure in such highly polluted regions. While some of the evidence in the individual studies is not conclusive[119], interesting points are raised with regards to the effect of the weather, gender and existing ailments. One paper highlighted a limitation of many investigations that was that the influence of the individual patient characteristics are largely ignored[120], meaning confounding variables could be influencing the conclusions.**

## 4.6 Diabetes in Adults

According to the International Diabetes Federation in 2011, diabetes effects at least 366 million people worldwide, and that number is expected to reach 566 million by the year 2030. Over 99% of all diabetes cases represent type 2:

While air pollution is said to be a risk factor for diabetes – epidemiological evidence is inconsistent and has not been systematically evaluated. A meta-analysis of 13 studies in Europe and North America concluded that existing evidence indicates a positive association between air pollution and diabetes mellitus (type 2) – but there is a high risk of bias[121].

> A study of African-American women from Los Angeles found that those who had higher exposure to traffic-related air pollutants ($PM_{2.5}$ and nitrogen oxides) were more likely to develop diabetes (as well as high blood pressure)[122]

> Adults in Denmark had an increased risk of diabetes when exposed to higher levels of the traffic-related air pollutant nitrogen dioxide ($NO_2$)-- especially those who had a healthy lifestyle, were physically active, and did not smoke-- factors that should be protective against type 2 diabetes[123].

> A study of adult women in West Germany found that women exposed to higher levels of traffic-related air pollution ($NO_2$ and PM) developed type 2 diabetes at a higher rate. This study followed the participants over a 16 year period (at the beginning, none had diabetes)[124].

> Another German study found that long-term exposure to PM increased the later risk of type 2 diabetes in the general population, as did living closer to a busy road[125].

> In Germany, those who lived near busy roads had twice the risk of type 2 diabetes over a 12 year period[126].

> A long-term study from Ontario, Canada, found that exposure to $PM_{2.5}$ was associated with the development of diabetes in adults[127].

> From Switzerland, a 10 year long study found that levels of $PM_{10}$ and $NO_2$ were associated with diabetes development in adults, at levels of pollution below air quality standards[128].

> A 30-year longitudinal study from Canadian women found that $PM_{2.5}$ levels were associated with diabetes (as well as stroke, congestive heart failure, and heart disease)[129].

> A shorter-term (12 month) study from the Northeast and Midwest U.S. did find an association between diabetes and residential proximity to a road (in women), although it did not find an association between diabetes and exposure to particulate matter in the year before diagnosis. The statistical analysis revealed slightly increased risk of diabetes to PM exposure, although the differences were not significant. This study used models based on people's addresses to estimate PM exposure, and did not measure exposure directly[130].

> Another 1 year-long study of elderly adults from Taiwan found that fasting blood glucose levels and hemoglobin A1c (HbA1c), a measure of average blood glucose levels over 3 months, were associated with exposure to particulate matter (both $PM_{2.5}$ and $PM_{10}$), ozone, and $NO_2$, but most strongly with particulate matter (higher blood pressure and total cholesterol levels were also associated with these pollutants[131]. In China, exposure to $NO_2$, $SO_2$, and $PM_{10}$ were associated with higher fasting blood sugar levels, especially in female, elderly, and overweight people[132].

*Publication example/s*

***Emerging data from both experimental and epidemiologic studies are beginning to provide insights into this association, but there are a number of areas that would benefit from further study. The societal costs of this link, if indeed true, are staggering given the ubiquitous nature of air pollution and the economic costs of obesity/diabetes related complications[133]. In addition – high-quality studies assessing dose-response effects are needed, specifically in developing countries[134].***

## 4.7 Neuro-function: Neurodevelopment and neurodegeneration

For the most part, current research and policy efforts link air pollution to respiratory and cardiovascular disease[135] – but there is a growing body of research linking it to neurodevelopment. A research study conducted under the BREATHE project explained that air pollution is regarded as a suspected developmental neurotoxicant[136]. The developmental processes of the human brain is complex and lengthy, and scientists are evermore interested in understanding external and environmental influences and their association to delays in cognitive development, with air pollution a suspected developmental neurotoxicant[137]. Long-term exposure to ambient air pollution is associated with cerebrovascular disease and cognitive impairment. However, it is not clear whether it is related to structural changes in the brain[138].

> A study researching exposure to fine particulates, residential proximity to major roads and measures of brain structure in nearly 1,000 men and women over 60 found that elevated $PM_{2.5}$ levels were associated with smaller total cerebral brain volume. While people naturally lose cerebral brain volumes as they get older, but these findings indicate that air pollution may speed up the process[139].

***Publication example/s***

An increased body of work show evidence linking air pollution to behaviour deficits, neuro-inflammation and neuropathology in human and animal studies[140], and these will be described below.

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### Dementia

Dementia has been one of the newest research findings into the health implications of air pollution exposure, with scientists beginning to understand whether and to what extent pollutants are capable of shrinking the brain and causing silent strokes[141], both of which are linked to dementia[142].

Furthermore, there is emerging evidence suggesting that living near major roads also might adversely affect cognition. However, little is known about its relationship with the incidence of dementia, Parkinson's disease, and multiple sclerosis. A 2017 study published in The Lancet[143] aimed to investigate the association between residential proximity to major roadways and the incidence of these three neurological diseases in Ontario, Canada in 6.6 million adults.

It was found that 1 in 10 dementia deaths in people living within 50 metres of a busy road were attributable to fumes and noise. The team tracked all adults aged between 20-85 living in Ontario from 2001 to 2012, more than 243,000 people developed dementia, 31,500 people developed Parkinson’s disease and 9,250 people developed multiple sclerosis. While there was no association between living near a road and Parkinson’s disease or multiple sclerosis, but there was an association with dementia. A linear decline in deaths was found the further people lived

away from heavy traffic, with a 7% higher risk in developing dementia among those living within 50 metres; a 4% higher risk at 50-100 metres and a 2% higher risk at 101-200 metres. After 200 metres there was no increase.

Leading on from this, a University of Southern California-led research project and the first of its kind in the US found that older women who live in places with fine particulate matter exceeding the US Environmental Protection Agency's standard are 81% more at risk for global cognitive decline and 92% more likely to develop dementia, including Alzheimer's. If their findings hold up in the general population, air pollution could be responsible for about 21% of dementia cases, according to the study. USC researchers and others in this field said more research is needed to confirm a causal relationship and to understand how air pollution enters and harms the brain. Accurate pollution monitors are important for this task.

> At The Beth Israel Deaconess Medical Centre, the same researchers who studied the effect of silent strokes - also researched cerebral brain volume and brain white matter volume in in the same participants, all of whom were free of dementia[144] [145]. Participant exposure to $PM_{2.5}$ through residential proximity to major roadways was measured against total cerebral brain volume with adjustments made for age, temporal and clinical trends and socioeconomic position. The results showed that a 20µg/$m^3$ increase in $PM_{2.5}$ was associated with a -0.32% smaller total cerebral brain volume[146], yet there was no pattern observed in the extensive white matter in the brain[147]. The study showed that higher levels of $PM_{2.5}$ exposure impacts the ageing of the structural brain, causing the brain to age by an extra year over a human lifetime[148], thus increasing the odds of experiencing more time with dementia and possibly a lower life expectancy.

***Publication example/s***

***To conclude, the latest research is pointing towards as casual relationship between pollution and dementia. One reason that it is of concern is that this could have detriment effects on memory and impairing thinking in middle-aged and older adults[149].***

## ANXIETY

Anxiety is the most common psychiatric disorder and globally affects around 16% of people at some point in life. It is associated with lessened productivity, increased medical care and risk of suicide.

> Whether there is a correlation between anxiety and exposure to air pollutants was the aim of a study published in the British Medical Journal in March 2015, conducted by the John Hopkins University and Harvard University. In this publication, scientists tested whether a higher risk of anxiety could be caused as a result of $PM_{2.5}$ to $PM_{10}$ exposure in a study of 71,271 women between 57-85 years of age[150]. The study concluded a considerable association between $PM_{2.5}$ exposure and anxiety risk, yet no link was found between anxiety risk and particulate matter larger than 2.5μm[151].

***Publication example/s***

***To conclude, (according to the authors above) particulate matter may trigger or worsen anxiety through oxidative stress and inflammation or deteriorate an existing health condition. However, this was merely an observational study, so no definitive conclusion can be drawn about cause and effect – highlighting the need for further research.***

## 5. Health Impacts on Children

It is important to distinguish this cohort of the population because, firstly they are one of the most vulnerable groups[152] and uniquely so (discussed later). Secondly, the effects of pollution on children may be long lasting as early-life illness may impede long-term development[153], and finally, we need to understand the risks to mitigate the negative effects.

A joint research project between Royal College of Physicians and Royal College of Pediatrics' and Child Health in 2016 stated that overall, the effects on children's heart, brain, hormone systems and immunity is proven and the effects on growth, intelligence, development of brain and co-ordination is still growing[154].

## 5.1 Respiratory System

Air pollution is increasingly known to impact the development of children's respiratory system after birth. There are several biological reasons[155] why young children's respiratory systems may be more susceptible to air pollution's effects:

1. Children's lungs continue to rapidly develop in the early years, and the cell layer lining the inside of the respiratory tract is particularly permeable during this age period.
2. Compared to adults, children have a larger lung surface area in relation to their body weight, and breathe 50% more air per kilogram of body weight.
3. The process of early growth and development is important for the health of the child in general, and therefore may also be a critical time when air pollution exposures can have lasting effects on future health.
4. Children tend to spend more time outdoors doing strenuous activities, such as playing sports, so they are breathing more outdoor air compared to adults.
5. Due to children's lungs not being completely developed, they may experience greater exposure to environmental pollutants than adults and the higher doses of varied composition may remain in their lungs for a greater duration[156].

Altogether, the negative effects of air pollutants on pulmonary function place children at a greater risk of air pollutant-induced exacerbation of asthma for the duration of their lives.

> The British Lung Foundation in 2011 suggested that breathing polluted air over several years could reduce the rate at which children's lungs grow[157]

> An article in the Economist in 2011 talked of the risk of pneumonia due to PM exposure, especially in children[158]

> An investigation of 2048 school children in Hong Kong found that children in high pollution districts had significantly lower complete speed and predicted maximal oxygen uptake, which is negatively associated with cardio-respiratory fitness, especially in girls[159]

> A 20 year Teplice Program in the Czech Republic found that an increased concentration of $PM_{2.5}$ and polycyclic aromatic hydrocarbons (PAHs) caused an increase in bronchitis in pre-school children. Even though the science behind this report is strong, it is important to bear in mind that these communities are heavy industry towns with coal mines, so the children would be a more/different risk to others in Europe and globally

> A 6-year study researching 2,400 children in 25 schools in East London concluded that those children living in highly polluted parts of cities to have up to 10% less lung capacity than normal, with warnings the damage could be permanent. This reduction could increase the risk of diseases such as asthma and bronchitis[160]

> There is a general consensus on the link between exposure to TRAP and increased risk of asthma, but the reported findings are not completely consistent. The diversity in findings may be partly explained by genetic variation between populations; therefore further investigations are required to explore the role of genetic variants[161].

> A study review[162] concluded that the outdoor air pollution affects the appearance and exacerbation of asthma in children. Although these findings are of great interest, the limitations of noted works make future investigations of the effect of air pollution on asthma in children essential.

*Publication example/s*

***The evidence covered above (and as quoted by the WHO) shows a relationship between exposure to ambient air pollutants and adverse effects on the development of lung function. Reversible lung function deficits, chronically reduced lung growth rates and lower lung function levels are associated with exposure to air pollution, as well as various illnesses including:***

- ***Pneumonia***
- ***Reduced cardo-respiratory fitness***
- ***Bronchitis***
- ***Asthma***

***Moreover, the evidence shows clearer relationships for particulate matter and traffic-related air pollution (indicated by nitrogen dioxide) than for other pollutants.[163]***

## 5.2 Neurochanges

Understanding the potential impact of air pollutants on the development of a child's brain is gaining increasing attention. A study by Harvard University[164] stated that:

"Air pollution contains many toxicants known to affect neurological function and to have effects on the foetus"

In this section, studies that focus on the effect of various pollutants on the brain of young children will be discussed, including publications discussing the impact of exposure to the foetus via maternal exposure. Topics covered include neurodevelopment, including delayed brain development and linking to symptoms of anxiety, depression, attention disorder, reduced IQ, ADHD and autism.

### The Developing Brain

Millions of children in polluted cities are showing detrimental brain effects but wide reaching public health initiatives targeting these populations are still considered premature or unwarranted. This is because the effects on children's central nervous system (CNS) not yet to be broadly recognized.

A meta-analysis released in 2014[165] demonstrated to the contrary – concluding that there is enough evidence supporting the perspective that the effects of air pollution on the brains of children and teens ought to be key public health targets.

> BREATHE (a 12-month research study) in Barcelona aimed to analyse children's developing brain, the superior working memory and attentiveness when exposed to higher or lower local traffic pollutants at school. The study took 2,715 children between ages seven and ten from 39 schools, who undertook computerised tests that took place once every 3 months over the course of a year[166].

The study concluded that those attending schools near busy roads and thus exposed to higher traffic-related air pollution, showed lesser improvements in cognitive development and only a 7.5% 12-month increase in working memory – compared to 11.5% for those who attended schools away from busy roads[167].

Children attending school in high polluted areas experienced a substantially smaller increase in all three cognitive measurements; attentiveness, brain development and memory. In this study the authors expressed that the accuracy of their findings could have been manipulated with other characteristics of the children, thus the findings merely suggest that the developing brain may be vulnerable to these toxic particulates during middle childhood.

***Publication example/s***

***To conclude, publications 'collectively suggest substantive effects that may have long-term clinical repercussions in terms of degenerative diseases. Given the social and economic burden of accelerated aging in our society, whose far-reaching ramifications are simply incalculable'.***

### AUTISM

Autism and autism spectrum disorders (ASD) are caused by disorders in the neurodevelopment of the brain and characterised by deficits in social interaction and communication and behavioural flexibility[168]. ASD, which tends to be developed during the third semester of pregnancy and first year of life[169], is showing an increase in reported prevalence worldwide[170].

More evidence is showing that environmental exposures, not only genetic causes are contributing factors for autism, particularly in utero or early life[171] [172]. Several studies have explored associations of air pollution with autism, suggesting that there are increased odds of having a child with autism when exposed to higher levels of PM[173], criteria pollutants[174], heavy metals such as mercury[175] and distance to major roads[176].

> A peer-reviewed independent report conducted by Europe PubMed Central (EPMC) examined the development of childhood autism and alteration of the Met genotype in the brain as a result of local traffic-related and regional sources of PM, $NO_2$ and $O_3$ exposure[177]. Analysis of the Met genotype was key as those who have the Met genotype have a higher risk of developing autism spectrum disorder. The EPMC found that those who had the MET genotype and were exposed to high levels of air pollutants experienced a higher risk of autism spectrum disorder compared with those with the same genotype and lower air pollution exposure. ASD was associated with "high" exposure to traffic-related air pollution including $PM_{10}$, $PM_{2.5}$ and $NO_2$, but not $O_3$[178].
>
> To conclude, From the 408 studied cases, the paper proved that living near a highly polluted road and thus suffer from unhealthy levels of traffic-related air pollution exposure, $NO_2$, $PM_{2.5}$ and $PM_{10}$ can alter the genetics of a child and increase their risk in developing ASD.

***Publication example/s***

***To conclude, since the associations discussed above are linking autism and ADHD with environmental variables, they warrant wider knowledge translation by and among the developmental, behavioural and clinical researchers and practitioners. In the future, this could affect how those children with a genetic disposition are bought up to ensure the best possible start in life.***

## 5.3 Diabetes and Obesity

Diabetes is a growing epidemic; both in developing and developed countries - despite this, diabetes itself remains somewhat of a mystery[179]. In recent years, studies have started linking air pollution to diabetes, with tests to find out whether pollutants can be the cause of earlier development of type 1 diabetes in children[180], this is compared to diabetes in adults, which was mainly linked to type 2. In addition to this, the childhood obesity epidemic is of huge concern, and while diet and a lack of physical activity has always been blamed – there is an emerging sector of research pointing to additional environmental factors.

> A 2002 pilot study in southern California detected whether $SO_2$, $NO_2$, $O_3$, $SO_4$ (sulphate), and $PM_{10}$ played a role in the development of diabetes in children under 5 years[181]. The conclusion was that increased ozone exposure may be a contributory factor to an increased incidence and $PM_{10}$ may be a specific contributory factor to the development of type 1 diabetes before 5 years.

> A follow up study in 2006[182] looked at the quantitate role of specific air pollutants. 402 children were studied (300 of them healthy, 102 diagnosed) all of whom were measured for their exposure to air pollutants over time, from birth-to-diagnosis, using zip code-specific pollution data and dividing it by the length of exposure. The study found that diagnosed had higher exposure to the pollutants $O_3$ and $SO_4$, as compared to healthy children with the strongest effect being ozone. The other air pollutants studied, namely $SO_2$, $NO_2$, and $PM_{10}$ were not associated with type 1 diabetes development[183].

> The Institute of Diabetes Research at the Helmholtz Centre analysed 672 diagnosed children to see whether there was a correlation between traffic related pollutants of less than 10µm and $NO_2$ accelerating its development[184]. The study took other environmental factors into consideration; namely history of diabetes in each patient's family, body mass index and education level of parents, and then compared exposure to air pollutants with the time of diagnosis. Those who have been exposed to high levels of local air pollution in residential environments were more prone to developing the condition three years prior to those who lived in lower polluted areas.

> A study from Chile looked at environmental ozone and $PM_{2.5}$ levels and the temporal patterns of Type 1 Diabetes in infants younger under age 15, to decipher whether the environmental factors could influence peaks of type 1 diabetes incidence in children. The researcher found that $PM_{2.5}$ levels were associated with the onset, which suggests that air pollution levels could be related to peaks of type 1 diagnosis[185]. There were also suggestions that certain influences could have impacted the results and were taken into consideration[186].

> A German project[187] identified that high exposure to $NO_2$ and larger/medium sized particulate matter, was linked to acceleration in the manifestation of type 1 diabetes in very young children[188].

> Near roadway air pollution exposure has been associated with increased body mass index and obesity in children, and excess weight gain in animal models. This emerging evidence of a broad spectrum of environmental chemicals having 'obesogenic' properties and altering the

metabolic profile of adipose tissue challenges the prevailing model that the childhood obesity epidemic is explained solely by increased caloric density of food and decreased physical activity[189].

***Publication example/s***

In addition to all the literature detailed above, recent emerging evidence suggests that air pollution exposure may contribute to the development of obesity and type 2 diabetes in children (as seen in adults). The objective of a University of Southern California led project[190] was to determine whether exposure to elevated concentrations of nitrogen dioxide (NO2) and PM2.5 had adverse effects on longitudinal measures of insulin sensitivity, β-cell function, and obesity in children at high risk for developing diabetes. Overweight and obese Latino children (8-15 years; 314 pupils) were enrolled from 2001 to 2012 in Los Angeles, and were followed up for an average of 3.4 years

By the time the participants turned 18, their insulin-creating pancreatic cells were 13% less efficient than normal, making these individuals more prone to eventually developing Type 2 diabetes, researchers said. This is the first to follow children for years to find a connection between air pollution and diabetes risk in children. When they turned 18, the participants had nearly 27% higher blood insulin after having fasted for 12 hours. During their two-hour glucose test, they had about 36% more insulin than normal, indicating that the body was becoming less responsive to insulin. This observation illustrated that increased exposure to air pollution was associated with increased risk factors for Type 2 diabetes.

***To conclude – it is apparent that air pollution exposure may be a predisposing, accelerating, or simply a surrogate factor in the development of type 1 diabetes in children[191]. The research discussed accredits the association with varying pollutants – showing the need for further research. Furthermore, the effects of air pollution on type 2 development in children is an emerging subject area requiring further understanding. Finally, further research is required into the effects of pollutant exposure on obesity levels in children – if environmental factors do increase obesity levels, this would have a huge impact on policy.***

## 5.4 Foetal Growth

As well as it being important to understand how a child's neurodevelopment is affected by external environmental chemicals during foetal development and in early growth years, it is also important to identify the potential effects of such chemicals on physical foetal growth.

Firstly, a literature review of 12 epidemiological investigations[192] (from 1987-2001) on the effects of ambient air pollution on foetal growth looked into low birth weight (LBW), preterm delivery (PTD) and intrauterine growth restriction (IUGR). The effects of air pollution were apparent on PTD and IUGR according to a study by the Teplice Program in the Czech Republic (detailed previously), which found an association between an increase in IUGR and PM 10 and PAHs exposure in the first month of gestation[193]. However, most of the associations reported were rather small and much smaller than the effects of other known risk factors.

This was backed up further by researchers for the Stockholm Environment Institute (SEI), the London School of Hygiene and Tropical Medicine and the University of Colorado[194] who concluded in 2017 that as many as 3.4 million premature births across 183 countries could be associated with $PM_{2.5}$ exposure, with sub-Saharan Africa, North Africa and south and East Asia most impacted by the issue. The substantial percentage of preterm births estimated to be associated with anthropogenic PM2.5 (18% (13%–24%) of total preterm births globally) indicates that reduction of maternal PM2.5 exposure through emission reduction strategies should be considered alongside mitigation of other risk factors associated with preterm births.

Furthermore, an association in the concerned literature review was not found with LBW. Despite this, it would be a cause of concern if prevalence of exposure is elevated to effect entire populations. There are issues associated with creating a summary of effects of the heterogeneity of studies with differences in measurements of outcome, exposure and confounders, and the fact that there are just a small number of studies per outcome. A similar systematic review of the epidemiological evidence into PM and foetal health in 2004 also looked at the conclusions of 12 studies and found little consistency in evidence linking PM and foetal outcomes, either finding small adverse effects or no effect at all. The review also concluded that many studies had methodological weaknesses in their design and adjustment for confounding factors[195].

In direct contrast to these literature reviews, there is evidence for more negative effects than previously stated. The effect of air pollution on foetal development is a complicated area to study, while previous studies have reported a decrease in birth weight with an increase in air pollution – it is not clear at what point during pregnancy exposure has the most effect[196]. In addition – studies have linked low birth weight to asthma and decreased lung function in adulthood[197].

> One study – published in 2015 – used the unusual circumstances around the Beijing Olympics to research just that, looking at more than 80,000 births. Beijing is 'one of the most heavily polluted cities in the world' and, as a condition for hosting the Olympics, had to combat their air pollution problem. They did so by temporarily closing factories, halting construction and

reducing the amount of cars on the road. The consequence was a reduction in air pollutants by between 18% and 59% during the 47 days of the games[198]. The conclusion of the study found that the greatest difference occurs during the 8th month of pregnancy – on average – babies were 23grams heavier compared to the same period in 2007 and 2009.

> Another paper talks of the risk that exposure to $PM_{10}$ and $O_3$ has during first trimester resulting in increases in blood pressure in the later stages of pregnancy (associations were stronger when restricted the analysis to non-smokers)[199].

> In a similar line, a Californian study investigating 298 pregnant women, mainly Hispanic, found exposure to CO and $PM_{2.5}$ in the first trimester was significantly associated with hypertensive disorder of pregnancy and these associations were modified by BMI (increased odds among non-obese women)[200]. Finally, a study using data from the EPA concluded that low air quality can lead to an increase in blood pressure within pregnant women, which can lead to complications that increase risks for mother and baby, such as preeclampsia[201].

> Also, a study of nearly 9400 infants in Southern California[202] (data collected by California Birth Defects Monitoring Program) found an odds ratio for cardiac ventricular septal defects increased with dose-response fashion with increasing 2nd month CO exposure. It also found risks for aortic artery and valve defects, pulmonary artery and valve anomalies and conotruncal defects increased with 2nd month $O_3$ exposure. However, it was inconclusive for other air pollutants. This was the first study of its time and recognised the need to be confirmed by further studies.

***Publication example/s***

Finally, a study[203] conducted in the US found that air pollution had a costly impact on unborn children, estimating that the economic impacts cost $4.33bn in 2010, of which $760 million were spent for medical care. PM2.5 may contribute substantially to burden and costs of PTB in the US, and considerable health and economic benefits could be achieved through environmental regulatory interventions that reduce PM2.5 exposure in pregnancy.

***One aspect to highlight in this section that, while meta-analysis of work are often the most reliable sources of information – the 2 discussed at the start use relatively old studies. Since 2004 (and earlier), there have been a lot of advances in research, and it would appear (using more recent literature) that there is a negative association present. This is of concern because, for example, children born at a clinically low weight are at greater risk of dying in infancy and are more susceptible to disease. Another reason this is of concern is that we do not know the long-term implication of these changes on the future health of the children[204]. So while it is a difficult aspect to measure, it is vital to do so to provide advice to expectant parents, especially when considering the economic impacts.***

# 6. EMERGING RESEARCH AREAS

## 6.1 HUMAN GENOME SYSTEM

In recent years publications have emerged with the aim to understand the effects of air pollution on the cells, genetic and DNA structure, yet the level of accuracy in these papers must be taken into account.

> A paper published by the Louisiana State University aimed to see whether environmentally persistent free radicals (EPFRs) cause damage to human cells[205]. The study divided a population of mice, with one group exposed to the EPFRs pollution. After infecting both groups of mice with a flu virus the scientists found that those exposed to the air pollutants were more defenceless to the virus, triggering immune cells that reduce the body's defence against infection[206]. In addition to this finding, the EPFRs also lowered the mice's ability to detoxify the harmful effects of the pollutant and cause an imbalance between the cell's ability to produce free radicals[207]. These results can have worrying effects on humans who have the flu and low defence to infections as it makes them more vulnerable, particularly those in infant years or of older age. It is important to note that this study was conducted on animals that may react differently to such external environmental factors than humans.

> In a paper published by the University of British Columbia, scientists hoped to understand whether air pollution affects the genetic composition in humans. A controlled human exposure was tested in a sealed 'smog booth' where they were exposed to traffic fume pollutants for two hours to look for changes in the human genome[208]. Blood samples were taken and 50,000 genes were examined before and after the experiment. Results showed that the pollutants did not cause any biological changes to the DNA structure, however, the layer of methyl molecules that sits over 400 of the genetic DNA had been altered and it is the DNA methylation patterns that are responsible for the working of genes. The study suggests that long-term exposures to air pollutants from fumes has the possibility to cause more fundamental accumulated biological effects than research has been shown thus far.

***Publication example/s***

***As an emerging research area, it is clear that there is need for further research topic as studies are starting to show that various levels of air pollution exposure can indeed alter some very important genetic makeup.***

## 6.2 Impacts on skin

The increase of air pollution over the years has major effects on the human skin. The skin is exposed to ultraviolet radiation (UVR) and environmental air pollutants such as polycyclic aromatic hydrocarbons (PAHs), volatile organic compounds (VOCs), oxides, particulate matter (PM), ozone (O3), and cigarette smoke. Although human skin acts as a biological shield against pro-oxidative chemical and physical air pollutants, the prolonged or repetitive exposure to high levels of these pollutants may have profound negative effects on the skin. Exposure of the skin to air pollutants has been associated with skin aging and inflammatory or allergic skin conditions such as atopic dermatitis, eczema, psoriasis or acne, while skin cancer is among the most serious effects.[209]

> A 2016 research project[210] studied people in both Germany and China and discovered that age spots on their cheeks increased by 25% with a relatively small increase in pollution, just 10 microgrammes of NO2 per cubic metre.

> Chronic exposure to traffic-related particulate matter (PM) was previously linked to development of facial lentigines in 400 Caucasian women from the Study on the Influence of Air Pollution on Lung Function, Inflammation and Aging (SALIA) cohort study.

***Publication example/s***

***While this area of research is not as severe or life threatening as other topics, it is important in terms of quality of life in high pollution areas. Appearance can have a huge impact on physiological health and self esteem, it should not be discounted.***

## 6.3 Drug resistant bacteria

Emerging research from the University of Leicester [211]has for the first time discovered that bacteria that cause respiratory infections can be directly affected by air pollution -- increasing the potential for infection and changing the effectiveness of antibiotic treatment. The interdisciplinary study has important implications for the treatment of infectious diseases that are known to be increased in areas with high levels of air pollution.

The research shows that black carbon changes the way in which bacteria grow and form communities, which could affect how they survive on the lining of our respiratory tracts and how well they are able to hide from, and combat, our immune systems. The research team found that black carbon alters the antibiotic tolerance of Staphylococcus aureus communities and importantly increases the resistance of communities of Streptococcus pneumoniae to penicillin, the front line treatment of bacterial pneumonia. Furthermore, it was found that black carbon caused Streptococcus pneumoniae to spread from the nose to the lower respiratory tract, which is a key step in development of disease. Staphylococcus aureus and Streptococcus pneumoniae, which are both major causes of respiratory diseases and exhibit high levels of resistance to antibiotics.

***Dr Julie Morrissey, the lead author of the paper, said: "Our research could initiate an entirely new understanding of how air pollution affects human health. It will lead to enhancement of research to understand how air pollution leads to severe respiratory problems and perturbs the environmental cycles essential for life."***

# 7. Conclusion

From the review above it is clear that there is a significant risk to human health from anthropogenic outdoor air pollution, and for a lot of the pollutants there is no safe level of exposure, even at the EU agreed level. The most conclusive health ailments, where the research is extensive and reaching similar conclusions, are the effects on life expectancy, cardiovascular health/stroke and lung cancer. On the other hand, it is clear that more recent studies on the effects on the respiratory system, and various developments in children such as links to diabetes, autism and other neuro-functions and developments are gaining increased interest and recognition. It is these more specific themes that may play a crucial role in the development of health care, health care expenditure and personal will to reduce exposure levels, for ones own health, that of our children within and out of the womb.

These negative associations between air pollution and health are particularly worrying because firstly, it affects all members of a population, and secondly there is an increase risk to vulnerable sectors including elderly, infant and those with existing conditions. A combination of an ageing, growing and higher urban population means that dealing with air pollution is a major challenge for this and future generations.

Despite all the research already conducted and mentioned above, there are many areas where there is yet to be a universal consensus drawn. One such area in need of development is the extent to which $PM_1$ impacts our health. There is a growing interest in understanding the amount and distribution of PM1 in our air and the link to the possible immense range of serious health conditions. However, this category of pollution has rarely been monitored, hindering the ability for scientists up until now to conduct research studies. Our concerns and the need for accurate research analysis requires fine-grain available data which covers entire cities or populations in sufficient detail, allowing precise conclusions to be drawn.

2016 marked the 60th anniversary of the Clean Air Act that was enacted by parliament after the 1952 London smog, which was responsible for over 4,000 deaths over a matter of days. While the scientific community is making significant progress in characterising pollutants, determining health effects and devising strategies, political and societal will is still lacking to create meaningful and positive change[212]. This needs to change rapidly, to protect the vulnerable, improve current quality of life and ensure the health of generations to come.

In terms of fuelling these meaningful and positive changes, the 'Every Breath We Take' report[213] summarises perfectly 14 key recommendations for the UK to increase awareness, manage exposure levels and reduce pollution levels overall. These 14 recommendations fall into the following 5 categories and these recommendations need to actioned now to safeguard to public:

1) **Education**: including healthcare professionals, Government representatives and the general public
2) **Regulation**: to put the onus on the worse polluters, enforce regulations and incentive industry

3) Monitoring and data: including accurate and wide-ranging programmes and to provide public alerts

4) Mitigation: tackle the inequality in impacts and protect those most at risk

5) Research and development: including health effects, economic impacts and the potential role of new technologies

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