Review and Assessment of the Evidence on Health Impacts of Low-Level Pollution in Countries with Levels of Ambient Air Pollution Comparable to Scotland

October 2023

Scottish Government
Riaghaltas na h-Alba

Report reference

RESAS/020/20 – Final Report, version 1.3

Contract Details

Scottish Government – Reference: RESAS/020/20 – Invitation to Tender: Provision of Review and Assessment of the Evidence on Health Impacts of Low-Level Pollution in Countries with Levels of Ambient Air Pollution Comparable to Scotland

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Abbreviations

BC – black carbon

CIND – cognitive impairment, not dementia

CO - carbon monoxide

CO_2 - carbon dioxide

CVD – cardiovascular disease

DALY - disability-adjusted life year

GNI - Gross National Income

HEI – Health Effects Institute

NO - nitric oxide

NOx - nitric oxides

NO_2 – nitrogen dioxide

O_3 – ozone

PAFs - population attributable fractions

PM – particulate matter

PM_{10} – particulate matter (particles are less than 10 micrometres in diameter)

$PM_{2.5}$ – particulate matter (particles are less than 2.5 micrometres in diameter)

QALY - quality-adjusted life year

RQ – research question

SDI – socio demographic index

SO_2 - sulphur dioxide

Contents

1 Background

The scope of the work commissioned under this specific request arises from the Cleaner Air for Scotland 2 (CAFS2) Strategy. One of the actions from the CAFS2 Strategy is to assess the evidence on health impacts of low-level air pollution in countries with levels of ambient concentrations comparable to Scotland. An earlier review by the CAFS2 Health Working Group identified an absence of evidence of association with cardiovascular disease (CVD) in Scottish studies. Part of the remit of this review is therefore to understand reasons for this apparent difference between health effects identified in Scottish studies and those in countries with levels of ambient air pollution comparable to Scotland. To review and assess the evidence of health impacts in such countries, a robust, rapid semi-systematic literature review was undertaken. This review aims to collate and discuss the evidence on:

- The health impacts of air pollution at low levels comparable to Scotland
- Reasons for an absence of association between air pollution and cardiovascular disease in Scottish studies.

2 Methodology

2.1 Literature search

A robust, rapid review of the available scientific literature was undertaken using the Scopus database. Due to the time and resource constraints of the study only Scopus was used, however Scopus is a relatively comprehensive database and additional searches were completed to ensure all relevant evidence was retrieved. Prior to the main literature search, a preliminary search was conducted using research databases and search engines. The purpose of this was to identify any important evidence that could frame the search strategy and terms. After the main literature search, supplementary searches using Google were conducted to ensure all relevant literature was obtained. Although the review is not a full systematic review, the search was conducted in a systematic way and using appropriate evaluation of the quality of sources to reflect the balance of evidence.

2.1.1 Search terms

The preliminary literature search identified a mapping review by Dominski *et al.* (2021) '*Effects of air pollution on health: A mapping review of systematic reviews and meta-analyses'*, herein referred to as the Dominski review. The Dominski review identified 240 evidence reviews that analysed the effects of air pollution on human health. The Dominski review is of important relevance to the research question and collates all the high-quality evidence synthesis papers published on or before 18 June 2020. However, to fully answer the research question, we have adapted the search terms in the Dominski review to collate evidence published after this date, as well as data that could be comparable to Scotland.

Table 1 provides a breakdown of the search terms used. Search terms [1] [2] and [4a] were based upon the terms used by the Dominski review (Dominski *et al*., 2021). The additional health search terms [3], were identified to encompass a wider range of both physical and mental health outcomes from air pollution. The search terms used to exclude weaker study designs [4b] were ascertained following in-depth discussions using the project team's subject area and methodological expertise and verified with Scottish Government. The timescale of the study [5] was designed to collect any new evidence, not published at the time of the Dominski review and the location [6] included countries comparable to Scotland, defined by population-weighted annual mean $PM_{2.5}$ data, from the Health Effects Institute's 2020 State of Global Air (Health Effects Institute, 2020). $PM_{2.5}$ was used as this pollutant is most commonly associated with health effects (UKHSA, 2022). To define countries as comparable to Scotland, data on the population-weighted mean exposure in either 2017, 2018 or 2019 (pre-COVID-19) was collected with a threshold of 12 $\mu g/m^3$, as the United Kingdom (including Scotland) mean is approximately 10.2 $\mu g/m^3$ (based on the State of Global Air 2017-2019 data). Finally due to the time implications of translation, only studies published in English language [7] were included. References and documents were stored and classified using Zotero reference management software.

2.1.2 Search limits

The search was limited to English language studies published between 1 January 2020 and 1 January 2024. Although the last search date in the review by the Dominski review is 18 June 2020, the search strategy used in this study was from 1 January 2020 to ensure all relevant papers were collated, including those that may have been accepted in early 2020 but not published until after 18 June 2020, due to the timescales associated with academic publishing. An end date of 1 January 2024 was used to capture any pre-dated early release publications.

Table 1: Search terms and combinations

Search terms	Descriptors	Justification	Reference
1. Air pollution	“air pollution” OR “air pollutant*” OR “air quality” OR “particulate matter” OR “PM10” OR “PM2.5” OR “carbon monoxide” OR “carbon dioxide” OR “ozone” OR “nitrogen dioxide” OR “sulfur dioxide” OR “traffic-related air pollution”	Based upon mapping review of systematic reviews/meta-analyses (Dominski review)	Dominski *et al.* (2021)
2. Physical health	“health” OR “public health” OR “cardiovascular disease” OR “ischemic heart disease” OR “cancer” OR “respiratory disease” OR “stroke” OR “cerebrovascular disease” OR “morbidit*”	Based upon mapping review of systematic reviews/meta-analyses (Dominski review).	Dominski *et al.* (2021)
3. Mental health and cognition	OR "anxiety" OR "depression" "cognit*" OR "memory" OR "cerebr*” OR “mental*" OR "declin*" or "deteriorat*" OR "degenerat*" OR "Neurodegenerative" OR "disorder" OR "neurological" OR "psych*"	Inclusion of wider health effects following discussion with Scottish government.	Zundel *et al.* (2022) Bui *et al.* (2018) Sun *et al.* (2015)
4a. Study type	“systematic review” OR “meta-analysis” OR “meta-analyses”	Based upon mapping review of systematic reviews/meta-analyses.	Dominski *et al.* (2021)
4b. Study type	AND NOT “case report” AND NOT “case-report” AND NOT "cross-sectional" AND NOT "cross sectional"		
5. Timescale	01/01/2020 – 01/01/2024	To collect new data, not encompassed by the mapping review of systematic reviews/meta-analyses.	Dominski *et al.* (2021)
6. Location	AND "American Samoa" OR "Andorra" OR "Australia" OR "Austria" OR "Bermuda" OR	Countries representative of ‘low-level pollution’. This is filtered from the	Health Effects

	"Brazil" OR "Brunei" OR "Darussalam " OR "Canada" OR "Cook Islands" OR "Denmark" OR "Estonia" OR "Fiji" OR "Finland" OR "France" OR "Germany" OR "Greenland" OR "Guam" OR "Iceland" OR "Kiribati" OR "Latvia" OR "Lithuania" OR "Luxembourg" OR "Maldives" OR "Marshall Islands" OR "Micronesia" OR "Monaco" OR "Nauru" OR "Netherlands" OR "New Zealand" OR "Niue" OR "Northern Mariana " OR "Norway" OR "Palau" OR "Portugal" OR "Puerto Rico" OR "Russian Federation" OR "Saint Kitts and Nevis" OR "Samoa" OR "San Marino" OR "Spain" OR "Sweden" OR "Switzerland" OR "Tokelau" OR "Tonga" OR "Tuvalu" OR "United Kingdom" OR "United States of America" OR "United States Virgin Islands" OR "Uruguay" OR "England" OR "Scotland" OR "Northern Ireland" OR "Wales" OR "USA" OR "Australasia" OR "Caribbean" OR "Eastern Europe" OR "High-income Asia Pacific" OR "High-income North America" OR "Oceania" OR "Southeast Asia" OR "Southern Latin America" OR "Tropical Latin America" OR "Western Europe"	2020nState of Global Air using $PM_{2.5}$ (which is most related to health effects) and setting a threshold of 12 $\mu g/m^3$ as the population-weighted exposure mean in any of the years 2017, 2018 or 2019 (pre-COVID-19). The UK mean is approximately 10.2 $\mu g/m^3$ for comparison. Independent Scottish data not available in this dataset.	Institute (2020)
7. Language	English		

3 Results

3.1 Search results

The final search was conducted on 6 June 2023, and a total of 333 studies were found using Scopus. The titles and abstracts were screened for relevance; 54 potentially relevant papers were identified, and full copies were obtained for detailed assessment. Of these, 46 papers were assessed as relevant and 8 were rejected. Papers were not included in the final analysis for the following reasons:

- The paper did not explicitly assess, analyse, or evaluate the association or impact of air pollution on human health.
- The level of evidence was not sufficient due to the methodological and data choices.
- The paper did not recognise or consider the role of confounding factors in their analysis.
- The interaction between air quality monitoring sites, and human geography was not appropriately considered or established.
- The paper was focused on evaluation of methodological/modelling choices, as opposed to air pollution and human health.

Additional search results were obtained during the preliminary and supplementary searches using the search engine Google and the Scopus database. This was to capture any relevant evidence not captured by the search strategy, including reports and research specific to Scotland that fell outside of the search timeframe. The Dominski review, three reports from the HEI and three papers (published before 1 January 2020) in Scotland were found.

3.2 Categorical breakdown of results

Table 2 to Table 8 show a categorical breakdown of the continent, country, age of participants, health outcomes, whether these outcomes were short-term or long-term, and the pollutants assessed in each of the studies, as well as the year of publication.

Half of the included papers (24/46) were from European countries, most commonly the UK (or England), Sweden, Denmark and the Netherlands. Around two-thirds of papers assessed health outcome in adults, with one third on health outcomes in children. The most evaluated health outcomes were mental health and well-being, dementia and cognition, with most papers focussing on long-term outcomes. It is worth recognising that the prevalence of papers on mental health and well-being is reflective of the search strategy timescale. The evidence on the physiological health impacts of air pollution has been established for several years. Therefore most of these papers would have been published prior to 1 December 2020 and the evidence from these studies will be captured by the mapping review by Dominski *et al.* (2020) and the three HEI reports. Of all pollutants $PM_{2.5}$ was the most evaluated, followed by NO_2 and PM_{10}.

Table 2: Geographic focus of relevant search results, by continent.

Continent	#
Europe	24
North America	10
Worldwide	6
South America	1
Australia	5
Total	**46**

Table 3 Geographic focus of relevant search results, by country.

Country	#
USA	6
n/a	6
Australia	5
Sweden	5
Canada	4
England	4
Denmark	3
Netherlands	3
UK	3
France	2
Germany	2
Brazil	1
Portugal	1
Spain	1
Total	**47**

Table 4 Demographic age focus of relevant search results.

Age	#
Adult	31
<18	15
Total	**46**

Table 5 Long- or short- term health outcomes assessed by relevant search results.

Health outcome duration	#
Long	39
Short	7
Total	**46**

Table 6 Categorical health outcomes assessed by relevant search results (primary results focus, overlap may exist within papers).

Health outcome	#
Mental health and well-being	11
Dementia	6
Cognition	5
Neurological	4
Respiratory	4
Development	3
Mortality	3
Cancer	2
Multiple	2
Neonatal	2
Diabetes	1
DNA methylation	1
Ocular	1
Primary care healthcare service use	1
Total	**46**

Table 7 Pollutants assessed[1] by relevant search results (count).

Pollutant	#
$PM_{2.5}$	41
NO_2	23
PM_{10}	19
O_3	13
NOx	11
Other	7
BC	3

Table 8 Year of publication relevant search results.

Year of publication	#
2020	1
2021	13
2022	19
2023	13
Total	**46**

[1] N.B. Studies evaluated one or more pollutants, hence the total for this table is greater than the number of included studies (n=47)

4 Discussion

This section discusses the evidence, starting with studies identified in the preliminary and supplementary searches in order of publication.

4.1 Health Effects Institute (HEI) reports

Along with the Dominski review, the preliminary searches identified three significant reports produced by the Health Effects Institute (HEI) assessing the health impacts of low-level air pollution. Whilst these reports are not peer-reviewed, they represent a scale and level of evidence that warrants their inclusion in this report; additionally, the countries of focus are broadly comparable to Scotland in terms of pollution levels and income (Gross National Income [GNI] per capita).

In 2014, the HEI issued RFA 14-3, '*Assessing Health Effects of Long-Term Exposure to Low Levels of Ambient Air Pollution'*. The three health effects studies included all-cause mortality, cause-specific mortality and morbidity endpoints (Health Effects Institute, 2014). Three teams were responsible for the research led by three principal investigators:

4.1.1 European HEI study, Dr Bert Brunekreef (Utrecht University)

The ELAPSE study analysed the health outcomes related to exposure to low ambient air pollution concentrations below international guidelines in Europe (based upon U.S. EPA National Ambient Air Quality standards (NAAQs), and WHO Air Quality Guidelines for annual average concentrations). The study developed new exposure models for Europe and identified four pollutants of interest, $PM_{2.5}$, BC, NO_2, and O_3, and analysed four categories of physical health outcomes, including natural and cause-specific mortality, coronary and cerebrovascular events, lung cancer incidence, and asthma and chronic obstructive pulmonary disease (COPD) incidence. They analysed data from 15 study (pooled) cohorts and seven large administrative cohorts, producing rich individual-level data for ~325,000 participants and a large sample size of ~28 million. Almost all participants (in 2010) had annual average exposures below the European Union limit values for $PM_{2.5}$ (25 µg/m^3) and NO_2 (40 µg/m^3), and about 14% had exposures below the NAAQs for $PM_{2.5}$ (12 µg/m^3)[2]. Within the pooled cohort the average pollutant exposures were 15 µg/m^3 $PM_{2.5}$, 1.5 × 10^{-5}/m BC, 25 µg/m^3 NO_2, and 67 µg/m^3 O_3. Among the administrative cohorts, mean concentrations of $PM_{2.5}$ ranged from 12 to 19 µg/m^3, except for the Norwegian cohort (8 µg/m^3).

The study found significant associations between $PM_{2.5}$, BC, and NO_2 exposure and natural-cause, cardiovascular, respiratory, and lung cancer mortality, as well as stroke, asthma, and COPD hospital admissions. The study also reported significant associations between NO_2 and acute coronary heart disease and between $PM_{2.5}$ and lung cancer incidence. The shape

[2] The current European Union limit values are equivalent to UK objectives ("The Air Quality Standards Regulations 2010," n.d.). The annual mean Air Quality Objectives for the protection of public health in Scotland are 10 µg/m^3 for $PM_{2.5}$ and 40 µg/m^3 for NO_2 (https://www.scottishairquality.scot/air-quality/standards)

of the associations between exposure and natural-cause mortality showed steeper slopes at lower exposures, indicating increased risks for mortality at even the lowest observed concentrations; furthermore there were no concentration levels where associations were not found for $PM_{2.5}$, BC, and NO_2 (Brunekreef *et al*., 2021).

Note: this study did not include data from Scotland. Furthermore, there is limited data from England due to complicated data privacy laws (Brunekreef et al., 2021).

4.1.2 Canadian HEI study, Dr Michael Brauer (University of British Columbia)

The MAPLE study examined whether exposure to $PM_{2.5}$ at concentrations below the current U.S. air quality standards (12 µg/m^3) was linked to an increased risk of nonaccidental death in 7.1 million Canadian adults. Satellite data, air quality monitoring data, and atmospheric modelling were combined to estimate outdoor $PM_{2.5}$ exposures across Canada from 1981 to 2016. In a large representative sample of Canadian adults, comprehensive epidemiological analyses were conducted to evaluate the risk of death at different $PM_{2.5}$ exposure levels and identify the lowest concentration at which associations with health effects could be detected. The results of the study found that long-term outdoor $PM_{2.5}$ exposures as low as 2.5 µg/m^3 were linked to an increased risk of death, with variation across different geographical regions and with smaller effects when adjusted for O_3 concentrations. The study identified associations with health effects at $PM_{2.5}$ concentrations below the current ambient air quality standard of 12 µg/m^3, suggesting that lowering the standard could yield further health benefits (Brauer *et al*., 2022).

4.1.3 American HEI study, Dr Francesca Dominici (Harvard University)

Dominici *et al.* (2019) examined the risk of mortality associated with exposure to low levels of ambient air pollution in 68.5 million older Americans (aged 65 and over). They created annual exposure models for three pollutants: $PM_{2.5}$, NO_2, and O_3, using a spatial resolution of 1 km x 1 km for the United States from 2000 to 2016. They used three causal inference approaches and two traditional regression approaches to analyse the data. They found that $PM_{2.5}$ was associated with an increased risk of all-cause mortality of 6% to 8% per 10 µg/m^3, which was consistent across all five approaches. The effect estimates were larger in a low-exposure sub-cohort. The consistency of the associations across the methods suggests that long-term exposure to $PM_{2.5}$ is likely to have a causal effect on mortality, providing stronger evidence than previous studies (Dominici *et al*., 2019).

4.2 Dominski mapping review

The preliminary literature search found an essential piece of literature which formed the basis for the main search strategy described in the methods. Dominski *et al.* (2021) provided a comprehensive mapping review of systematic reviews and meta-analyses that assessed the relationship between air pollution and human health. They identified 240 relevant papers published globally, with most of the selected studies carried out in North America (n = 93), followed by Europe (n = 85), and Asia (n = 85). The majority of these geographies are broadly similar to Scotland in levels of air pollution. The total sample size considered in the reviews was 118,113,670 (123 reviews reported), with a mean of 960,273 (minimum of 376 and maximum of 28,215,394 people) and ages ranged from 0 to 120 years.

The Dominski review investigated five research questions (RQs):

1. RQ1. How many systematic reviews (SRs) and meta-analyses (MAs) have been published on the effects of air pollution on health? Is there any temporal trend? What is the geographical distribution of the authors?
2. RQ2. What methodological characteristics did the SRs and MAs present?
3. RQ3. What were the most commonly investigated health outcomes?
4. RQ4. Which air pollutants and environments were most commonly investigated?
5. RQ5. What is the relationship between health outcomes and air pollutants?

Regarding RQ5, concerning the relationship between health outcomes and air pollutants, 75% of reviews (180/240) showed a positive association, 53/240 (22%) studies were classified as ambiguous and only seven (3%) showed a negative association or no harmful effect(s). Of these seven the health outcomes they analysed were: asthma, childhood cancer, congenital heart defects, pneumonia, stroke, telomere length, and venous thrombosis.

Overall, the review found that exposure to air pollution is associated with a range of adverse health outcomes. The studies suggest that even low levels of PM exposure can increase the risk of respiratory and CVD, cancer, and premature death. Exposure to $PM_{2.5}$ was the most widely studied pollutant and an association was found with 8/10 health outcomes evaluated. The most frequently studied health outcome was CVD (32 reviews).

4.3 Discussion of results by health outcome

The order of the following sections is based upon the volume of evidence identified by the search strategy in this review. Therefore, this order does not necessarily reflect the body of evidence before 1 January 2020, nor does it reflect the potential public health impact or importance.

4.3.1 Cardiovascular disease (CVD)

As described in section 3, the results of the literature search only produced one paper that specifically looked at CVD, however this is likely an artefact of the search timeframe. The paper identified by the search strategy was So *et al.* (2022), which analysed the data from all Danish residents aged 30 and above (n=3,083,227). They found that long-term exposure to $PM_{2.5}$ (mean: 12.4 µg/m^3), NO_2 (20.3 µg/m^3), and/or BC (1.0×10^{-5}/m) was statistically significantly associated with all studied mortality outcomes (except for chronic kidney disease). Furthermore, their analysis showed that a 5 µg/m^3 increase in $PM_{2.5}$ was associated with higher mortality due to CVD (1.09; 1.07-1.12) (So *et al*., 2023). This mirrors the evidence collated by Dominski *et al.* (2020) which presented several systematic reviews and meta-analyses, all of which showed that an increase in the concentration of particulate matter is associated with CVD and mortality, in the short- and long-term. The most commonly reported associated outcomes were ischemic heart disease, heart failure, ischemic stroke, and arrhythmia. Additionally, Brunekreef *et al.* (2021), Dominici *et al.* (2019) and Brauer *et al.* (2022) all report a significant positive association between air pollution, CVD, and mortality. This significant association on a combined sample of over 103 million shows the overwhelming consensus of evidence that air pollution is associated with both CVD and mortality.

Whilst the three HEI reports, the Dominski review, and the evidence identified by this review all provide significant evidence for the association and impact of air pollution on cardiovascular health globally, the current evidence available in Scotland is not conclusive. There are three published research papers that analyse the health impacts of low-level air pollution in Scotland – Yap *et al.* (2012), Willocks *et al.* (2012) and Lee *et al.* (2019), the latter two papers found no association between air pollution and CVD, which contrasts with most of the evidence globally.

Yap *et al.* (2012), investigated the association between exposure to black smoke (BS) air pollution and mortality in two Scottish cohorts over a 25-year period. The results show consistent associations between BS and mortality and more specifically significant associations with all-cause mortality, cardiovascular mortality, ischaemic heart disease and respiratory mortality. None of these associations were affected by adjustment for area-level deprivation but all were associated with inverse-distance monitoring, meaning the further the individual lived from the air pollution source the smaller the association. These results are consistent with the global evidence that air pollution has negative effects on human health, including CVD.

In contrast to Yap *et al.* (2012), Willocks *et al.* (2012) and Lee *et al.* (2019) found no association between air pollution and CVD in Scotland. Willocks *et al.* (2012) used an ecological time-series design, and an over dispersed Poisson log-linear model to examine if there is evidence of an association between short-term exposure to particulate matter (PM_{10}) and hospital admissions due to CVD, in Edinburgh and Glasgow during 2000 to 2006. The pollution data were lagged, relative to the admissions data, to ensure that the exposure occurred before the response. The results of this analysis showed no consistent associations between PM_{10} concentrations and cardiovascular hospital admissions as all the estimated relative risks were close to one, and all but one of the associated 95% confidence intervals contained the null risk of one.

However, the absence of evidence of an association in this study does not prove that there is no association. The wider literature, from countries similar to Scotland, establishes a strong association between CVD and air pollution, both in the short- and long-term (Brunekreef *et al*., 2021; Dominski *et al,* 2020). The absence of an association found by Willocks *et al.* (2012) may be due to several limitations in their methodology. Firstly, they only collected data on PM_{10}, therefore the full spectrum of air pollutants that are harmful to human health and linked to CVD are not considered. For example, $PM_{2.5}$ has been shown to be more strongly associated with adverse health outcomes than PM_{10} (UKHSA, 2022). This in part is because $PM_{2.5}$ has a smaller diameter and can therefore penetrate deeper into the lungs and cross into the bloodstream. Additionally, BC, NO_2, and O_3 have all been strongly associated with adverse health outcomes including CVD. In addition to the absence of data on other important pollutants, the data on PM_{10} is incomplete. On 12.9% (Edinburgh) and 1.1% (Glasgow) of days no PM_{10} measurements were available. As a result, Willocks *et al.* (2012) only used data for days where at least one pollution measurement was available. The monitoring data was downloaded from the Scottish Air Quality website from sites throughout Scotland. Whilst the incomplete data poses issues around spatial representivity of the monitoring data compared to the population data, incomplete air pollution monitoring data is a common occurrence throughout the wider literature (Chastko and Adams, 2019), and does not negate the relevance of the research. The authors also discuss the possibility that the study design did not provide enough statistical power to detect a pollution-health relationship. The number of CVD admissions was relatively low – interquartile range (IQR) 4 to 8 cases per day in Edinburgh, and between 8 and 13 cases per day in Glasgow. Finally, the study only analysed hospitalisations and the long-term effects of air quality on CVD were not discussed, despite being widely accepted and documented elsewhere in the literature (Willocks *et al*., 2012).

Lee *et al.* (2019) reviewed the epidemiological evidence quantifying the health impact of air pollution in Scotland. They analysed the relationship of four pollutants (PM_{10}, $PM_{2.5}$, NO_2, and NOx) against cardio-respiratory disease and total non-accidental mortality outcomes. The study used data from mainland Scotland across a two-year period (2015-2016) with the study region spatially partitioned into 1,252 Intermediate Zones (IZ). The results show that all pollutants exhibit significant associations with respiratory disease but not CVD.

When evaluating the absence of the association with CVD it is important to consider how the authors analysed the effects of confounding factors. Lee *et al.* (2019) discuss smoking, which has been widely evidenced to affect cardio-respiratory disease incidence. Data on smoking prevalence was not available at IZ scale so their model used the Scottish Index of Multiple Deprivation (SIMD) score as a proxy for smoking. The justification for this decision is a paper by Kleinschmidt *et al.* (1995), however the current (2019) association between smoking and socio-economic status was not discussed and therefore this may have affected the validity of the analysis. The Scottish Health Survey (2021) shows that the age-standardised prevalence of current smoking status was higher among adults living in more deprived areas than among those living in less deprived areas (24% and 5%, respectively). This pattern has been evident since 2003 in the Scottish Health Survey data, and for longer elsewhere, however, all categories of deprivation have seen a reduction in smoking rates over time. Whilst the association between smoking status and socio-economic status cannot be refuted, the strength of the association has changed over time. There is no evidence that CVD or total non-accidental mortality are associated with any of the four pollutants, as the 95% credible intervals contain the null risk of one, and the estimated risks are mostly very close to one. However, it is possible that the adjustment for confounders may be oversensitive due to the historic data used to quantify the association. The confounders, including SIMD, were retained in all models but the significance of these variables is not stated (Lee *et al*., 2019).

In conclusion, whilst Willocks *et al.* (2012) and Lee *et al.* (2019) did not find an association between air pollution and CVD, this is likely an artefact of the study design and data. These limitations explain in part why the results are different from the earlier research by Yap *et al.* (2012) and the vast consensus of global research and data.

4.3.2 Mental health and well-being

As stated, the most evaluated health outcome in our search results was mental health and well-being, and this is likely reflective of the search strategy timescale. The evidence on the physiological health impacts of air pollution has been established for several years, therefore the majority of these papers would have been published prior to 1 December 2020. The timescale of this search evidences the increased focus on research investigating the relationship between other health outcomes, including mental health and well-being, in recent years. There is a good body of evidence on the association between air pollution and mental health and well-being and studies have consistently shown that exposure to air pollutants is linked to various negative mental health outcomes.

The search identified three studies which analysed the association between air pollution and mental health and well-being, specifically in individuals aged 18 or younger. Mok *et al.* (2021) analysed a cohort of individuals born in Denmark between 1 January 1979 and 31 December 2006 (n = 1,424,670), with information on estimated daily exposures to $PM_{2.5}$ and NO_2 at residence from birth to their tenth birthday. They found that higher exposure to $PM_{2.5}$ and NO_2 during childhood increased the risk of self-harm. Specifically, the risk of self-harm was elevated by 1.45-fold for individuals exposed to 17–19 $\mu g/m^3$ of $PM_{2.5}$ on average per day and by 1.59-fold for those exposed to higher levels (>19 $\mu g/m^3$), when compared with a mean daily exposure of <13 $\mu g/m^3$. In addition, higher mean daily exposure to NO_2 was associated with increased self-harm risk, but the dose-response relationship observed was less clear than for $PM_{2.5}$ (Mok *et al*., 2021). Two other studies (Reuben *et al.,* 2021; Latham *et al.,* 2021), used data from the Environmental-Risk Longitudinal Twin Study, a population-based cohort study of 2,232 children born between 1 January 1994 and 4 December 1995 across England and Wales to analyse the impact of air pollution on mental health and well-being. Reuben *et al*. (2021) discovered that higher levels of outdoor NOx exposure during adolescence were associated with a greater impact on psychopathology during the transition to adulthood. This suggests that NOx may be a nonspecific risk factor for the development of psychopathology (Reuben *et al*., 2021). Latham *et al*. (2021) identified a higher risk of major depressive disorder in adolescents with greater exposure to NOx and $PM_{2.5}$. The risk of major depressive disorder was highest for participants within the top quartile of annual exposure to NOx (adjusted OR = 1.43) and $PM_{2.5}$ (adjusted OR = 1.35). This indicated the potential role for childhood ambient air pollution exposure in the development of adolescent major depressive disorder (Latham *et al*., 2021).

In conclusion, this evidence suggests that air pollution has significant implications for mental health and well-being in individuals aged 18 or younger. Whilst further research is needed to better understand the mechanisms underlying these associations and inform effective interventions, exposure to air pollution during childhood/adolescence is associated with the development of mental health conditions and there is a need to mitigate the adverse effects.

This association has also been investigated in adults. Li *et al.* (2023) used data collected between March 2006 and October 2010 from 354,897 participants aged 37 to 73 years from the UK Biobank. During a median follow-up of 9.7 years, they observed that $PM_{2.5}$ and NOx were associated with an increased risk of major depressive disorder. Specifically, each 5 $\mu g/m^3$ increase in $PM_{2.5}$ was associated with a hazard ratio of 1.16, and each 20 $\mu g/m^3$ increase in NOx was associated with a hazard ratio of 1.02 for major depressive disorder. There was also a significant interaction between genetic susceptibility and air pollution, indicating that individuals with high genetic risk and high $PM_{2.5}$ exposure had the highest risk of developing major depressive disorder. Additionally, there was an interaction between $PM_{2.5}$ exposure and an unhealthy lifestyle, with participants having the highest major depressive disorder risk when they had both the least healthy lifestyle and high air pollution exposures (D. Li *et al*., 2023). Petrowski *et al.* (2021) investigated the effects of air pollution, specifically PM_{10}, on determinants of mental health and well-being, measured by life satisfaction, stress resilience, anxiety, depression, and self-esteem, in a representative sample of 3,020 German adults. A multivariate linear regression analyses show that higher life satisfaction, more self-esteem and higher stress resilience are predicted by less air pollution (PM_{10}). Confounders including individual income, age, and gender were adjusted for (Petrowski *et al*., 2021). Similarly, outcomes from "Understanding-Society: The-UK-Household-Longitudinal-Study" were linked to air pollution data and showed that with every 10 $\mu g/m^3$ increase NO_2, SO_2, PM_{10} and $PM_{2.5}$ the likelihood of poor mental well-being increased. Additionally, living in more polluted local authorities (SO_2, PM_{10}, and $PM_{2.5}$) as well as belonging to a non-UK born ethnic group increased the odds of poor mental well-being (Al Ahad *et al*., 2022). In conclusion, the research identified also provides positive evidence of the association between air pollution and mental health and well-being in adults. These findings underscore the importance of addressing air pollution as a potential risk factor for mental health issues in both adults and children.

There is also evidence for short-term associations between air pollution and mental health and well-being. Newbury *et al.* (2021) used a retrospective cohort study to assess the longitudinal association between air pollution exposure and mental health service use among individuals with first presentations of psychotic and mood disorders. Between 2008 and 2012, 13,877 individuals (≥15 years) had first contact with the South London and Maudsley NHS Foundation Trust for psychotic and mood disorders. High-resolution estimates of NO_2, NOx, $PM_{2.5}$ and PM_{10} were linked to the individual's residential address. Interquartile range increases in NO_2, NOx and $PM_{2.5}$ were associated with 18%, 18% and 11% increased risk for in-patient days respectively. Similarly, interquartile range increases in NO_2, NOx, $PM_{2.5}$ and PM_{10} were associated with 32%, 31%, 7%, and 9% increased risk respectively for community mental health service events after 1 year, and these associations persisted after 7 years. This analysis indicates that there is an association between residential air pollution exposure and increased mental health service use among people recently diagnosed with psychotic and mood disorders (Newbury *et al*., 2022). Qiu *et al.* (2022) also analysed the effects of short-term increases in air pollution ($PM_{2.5}$ and NO_2) on acute psychiatric hospital admissions, but in adults aged 65 years and older in the USA. They observed that short-term increased exposure is associated with increased risk of acute hospital admissions for psychiatric disorders. For every 5 µg/m^3 increase in $PM_{2.5}$, there is a corresponding increase in hospital admission rates of 0.62% for depression, 0.77% for schizophrenia, and 1.19% for bipolar disorder. Similarly, for every 5 parts per billion (ppb) increase in NO_2, there is an increase in hospital admission rates of 0.35% for depression and 0.64% for schizophrenia (Qiu *et al*., 2022). A study analysing air pollution and psychiatric emergency room visits in Sweden also demonstrated a significant association between air pollution and an increased number of psychiatric emergency room visits, specifically $PM_{2.5}$ and NO_2. Furthermore, the study identified individuals with pre-existing mental health conditions, males, and individuals aged 65 or older as groups with increased susceptibility (Muhsin *et al*., 2022). Following coal mine fires in Australia, Carroll *et al.* (2022) looked specifically at the impacts of $PM_{2.5}$ levels on the utilisation of ambulance and hospital services for mental health conditions in the local population. They found that $PM_{2.5}$ exposure was associated with an increase in access for mental health services. Specifically, a 10 µg/m^3 increase in daily $PM_{2.5}$ was associated with a 38% rise in ambulance attendances for anxiety and a 26% rise in emergency department presentations for depression. This suggests that health services should expect to have an increase in the number of people seeking assistance for mental health conditions during extreme air pollution events (Carroll *et al*., 2022).

Alongside the general link between air pollution and mental health and well-being, evidence indicates a clear link between air pollution and short-term mental health and well-being. Studies examining different populations, including individuals with first presentations of psychotic and mood disorders, older adults, air pollution events, and psychiatric emergency room visits, consistently show associations between residential air pollution exposure and increased mental health service use.

While causality cannot be assumed, the evidence clearly indicates an association between air pollution and negative effects on mental health and well-being in a wide variety of populations and settings. These findings emphasize the importance of addressing air pollution as a significant environmental factor affecting mental health and well-being.

4.3.3 Dementia

Multiple studies have provided evidence linking air pollution to the development and exacerbation of dementias. In the French population-based cohort known as the 3C Study, an association was found between $PM_{2.5}$ exposure and various forms of dementia, including all-cause dementia, Alzheimer’s disease, and vascular/mixed dementia. Specifically, for every 5 µg/m^3 increase in $PM_{2.5}$, the hazard ratio was 1.20 for all-cause dementia, 1.20 for Alzheimer's disease, and 1.33 for vascular/mixed dementia. However, no significant association was observed between NO_2 or BC exposure and dementia risk in this study (Mortamais *et al*., 2021). Similar findings were reported in Sweden by Kriit *et al*. (2021), who estimated that 5% of annual dementia cases in Sweden were attributable to $PM_{2.5}$ exposure, equating to 820 cases per year.

In the UK Biobank data analysis, which included a large sample size of 187,194 individuals, consistent associations were observed between $PM_{2.5}$ exposure and increased risk of all-cause dementia and Alzheimer's disease. Specifically, each increase in $PM_{2.5}$ was associated with a hazard ratio of 1.17 for both all-cause dementia and Alzheimer's disease. $PM_{2.5}$ is not the only air pollutant which is associated with dementia. NO_2 exposure was found to be associated with a higher risk of any incident dementia, Alzheimer's disease, and vascular dementia (n= 187,194) (Parra *et al*., 2022).

Further evidence from the Betula project, a longitudinal study on aging, memory, and dementia in Sweden, demonstrated that every 1 $\mu g/m^3$ difference in annual mean $PM_{2.5}$ concentration was associated with a hazard ratio of 1.23 for dementia after adjusting for factors including age, sex, apolipoprotein E (APOE) gene (a risk factor for Alzheimer's disease), Scandinavian Odor Identification Test (SOIT), cardiovascular diseases and education (Andersson *et al*., 2023).

As well as the association between air pollution and dementia incidence, air pollution has been evidenced to exacerbate symptoms of Parkinson's disease. An analysis of hospital admission data from 18 French areas showed a small but significant influence of PM_{10}, $PM_{2.5}$ and NO_2 on all-ages Parkinson's disease hospital admissions, indicating that air pollution contributes to the worsening of Parkinson's disease symptoms (Goria *et al*., 2021).

Zhao *et al.* (2021) assessed the relationship between O_3 exposure and mortality attributable to four neurological diseases, including Parkinson's disease and dementia. Their analysis utilised data from the 2001 Canadian Census Health and Environment Cohort, comprising 3.5 million adults with a combined follow-up of 51,045,700 person-years. The results demonstrated positive associations between O_3 exposure and mortality from Parkinson's disease and dementia, even after adjusting for demographic, socioeconomic, environmental, and contextual factors. Specifically, each interquartile range increase in O_3 (10.1 ppb) was associated with hazard ratios of 1.09 for Parkinson's disease and 1.08 for dementia. Between 2001 and 2016, 5.7% and 5.0%, of deaths from Parkinson's disease and dementia, respectively, were attributable to O_3 exposure (N. Zhao *et al*., 2021). The other neurological outcomes assessed are discussed in section 1.4.5..

In summary, multiple studies identified in this review provide consistent evidence linking air pollution, particularly $PM_{2.5}$, to an increased risk of dementia and potentially the exacerbation of Parkinson's disease symptoms. These findings underscore the importance of addressing air pollution as a public health concern and mitigating the burden of these neurodegenerative conditions.

4.3.4 Cognition

This review identified several publications that demonstrate the detrimental effects of air pollution on cognition across various populations and age groups.

Thompson *et al.* (2023) conducted a systematic review and meta-analysis that identified and analysed eighty-six studies assessing the effects of air pollution on cognition including attention, memory, language skills, and academic performance. Whilst the literature identified was contradictory there is moderate evidence for harmful associations between $PM_{2.5}$ and general cognition in adults over 40 years old. Additionally, they found associations between $PM_{2.5}$, NOx, and PM_{10} exposure with executive function, particularly working memory, in children. Furthermore, O_3 was associated with general cognition in adults aged 40 and above, while NOx showed links with reasoning/IQ in children. Moreover, a 1 $\mu g/m^3$ increase in $PM_{2.5}$ was significantly associated with lower verbal fluency and decreased performance in executive function tasks (Thompson *et al*., 2023).

As with dementia, the harmful effects of air pollution on cognition and dementia are evident. Wu *et al.* (2022) use data from the Swedish National Study on Aging and Care in Kungsholmen (SNAC-K) (n= 1,987) to demonstrate the harmful effects of long-term exposure to ambient air pollutants incidence of cognitive impairment, not dementia (CIND). Their analysis showed that a 1 $\mu g/m^3$ increase in $PM_{2.5}$ exposure was associated with a 75% increased risk of incident CIND, while weaker associations were found for PM_{10} (hazard ratio for 1-$\mu g/m^3$ = 1.08) and NOx (hazard ratio for 10 $\mu g/m^3$ = 1.18). Interestingly, they demonstrate that air pollution is a risk factor for the progression of CIND to dementia. Grande *et al*. (2021) also analysed SNAC-K data and found an association between air pollution, particularly $PM_{2.5}$ up to 8.6 $\mu g/\ m^3$, and cognitive decline. They also observed that the presence of cerebrovascular diseases further amplified the risk associated with air pollution by 6% (Grande *et al*., 2021).

Examining the combined effects of air pollution and deprivation on cognition, Christensen *et al*. (2022) analysed data from the Emory Healthy Aging Study (EHAS) comprising 11,897 participants aged 50 years and above. They observed that individuals residing in areas with higher air pollution concentrations and higher deprivation levels exhibited higher cognitive function instrument (CFI) scores, indicating increased perceived memory and cognitive decline. Notably, even after accounting for confounding factors related to deprivation, there were clear synergistic effects of air pollution and deprivation on cognition (Christensen *et al*., 2022).

The detrimental effects of air pollution on cognition extend to prenatal exposure. Zhang *et al*. (2022) examined 348 mother-child dyads from New York City and Boston, assessing the associations between prenatal $PM_{2.5}$ exposure and childhood cognition. The study found associations between $PM_{2.5}$ exposure during the third trimester of pregnancy and cognition scores in children, with variations observed based on location and child sex. The pooled analysis also indicated that maternal education and urbanicity may modify the association between prenatal $PM_{2.5}$ exposure and childhood cognition (Zhang *et al*., 2022).

Like deprivation, residential greenness was found to play a role in the relationship between air pollution and cognition. Wang *et al*. (2023) utilised data from the Longitudinal Study of Australian Children, involving 6,220 adolescents and 2,623 mid-life adults to assess the effects of air pollution and greenness on cognitive function, working memory and executive function. Within the adolescents, an IQR increase of NO_2 was associated with increased odds (19–24%) of having poorer executive functions, associations weren't observed between air pollution and other outcomes. For the adults, high NO_2 exposure predicted poorer cognitive function across all outcomes, while high $PM_{2.5}$ predicted poorer attention only. Increased levels of residential greenness were associated with better executive function in the minimally adjusted models for both adolescents and adults. However, these associations disappeared when fully adjusted for other factors, indicating that while residential greenness may have some positive effects, it does not eliminate the harmful association between air pollution and cognition (Wang *et al*., 2023).

In summary, the papers identified support the harmful effects of air pollution on cognition across various populations, including adults, children, and individuals exposed prenatally. Studies consistently demonstrate associations between air pollution exposure and cognitive impairments, including attention, memory, language skills, and academic performance. This emphasises the need for effective strategies to reduce air pollution and mitigate impact on cognitive health across population groups.

4.3.5 Neurological

As discussed in section 1.4.3, alongside cognitive and dementia health outcomes, the wider neurological effects of air pollution have been assessed. Zhao *et al.* (2021) assessed the relationship between O_3 exposure and mortality attributable to neurological diseases. Their analysis utilised data from the 2001 Canadian Census Health and Environment Cohort, comprising 3.5 million adults with a combined follow-up of 51,045,700 person-years. The results demonstrated positive associations between O_3 exposure and mortality from four neurological diseases (Parkinson's disease, dementia, stroke and multiple sclerosis), even after adjusting for demographic, socioeconomic, environmental, and contextual factors. Specifically, each interquartile range increase in O_3 (10.1 ppb) was associated with hazard ratios of 1.06 for stroke and 1.35 for multiple sclerosis. Notably, the significance of these associations was unaffected by most covariates, except for adjustment for Canadian regions. Between 2001 and 2016 3.8% and 19.1% of deaths from stroke and multiple sclerosis, respectively, were attributable to O_3 exposure (N. Zhao *et al*., 2021).

Research also suggested that air pollution, including CO, NO_2, SO_2, O_3 and $PM_{2.5}$, are associated with an increased number of emergency department visits for nervous system disorders. The analysis used data from a large Canadian city between 2004 and 2015 and demonstrated that increased levels of ambient CO, $PM_{2.5}$, and SO_2 were linked to an elevated risk of emergency department visits for episodic and paroxysmal diagnoses, particularly migraines. This association was observed at various time lags between 0-15 days, with significant effects observed on days 1, 6, and 7 following exposures (Lukina *et al.*., 2022). Similarly Min *et al.* (2023) analysed data from New York and found that a 1 $\mu g/m^3$ increase in $PM_{2.5}$ (lagged 0-1 years) was associated with an increased risk of headache and convulsion by 1.06 and 1.04, respectively (Min *et al*., 2023). This evidence highlights the short-term impact of ambient air pollution on neurological health.

Other neurological conditions linked to air pollution include autism spectrum disorder and attention deficit hyperactivity disorder. Li *et al.* (2023) analysed data from a longitudinal study of 2,750 children in the Netherlands and found evidence that higher levels of exposure to PM were associated with more severe autism spectrum disorder and attention deficit hyperactivity disorder symptoms. While no other associations were observed, this research provides some evidence about associations between PM and neurodevelopmental diseases among adolescents (Y. Li *et al*., 2023).

The evidence presented in this section provides further evidence of the link between air pollution and Parkinson's disease, dementia and stroke, and evidence of an association with other neurological outcomes including multiple sclerosis, emergency department visits for nervous system disorders, autism spectrum disorder and attention-deficit/hyperactivity disorder in children. These findings highlight the detrimental effects of air pollution on neurological health, both in terms of mortality and the incidence and severity of neurodevelopmental and neurological disorders.

4.3.6 Respiratory

Numerous studies have investigated the relationship between air pollution and respiratory health. The Dominski review notes that most of the research has focussed on respiratory health outcomes, with harmful effects being described and evidenced in a wide range of populations and for a range of respiratory outcomes. This report identified four additional studies investigating this association.

Anenberg *et al.* (2022) considered the effects of air pollution on paediatric respiratory health. Using existing global annual average NO_2 concentration datasets for 2010-2012 they linked and compared these to population and baseline asthma rates to estimate NO_2 attributable paediatric asthma incidence. Their analysis estimated that 1.85 (95% CI 0.93-2.80) million new paediatric asthma cases were attributable to NO_2 globally in 2019, with two thirds of these occurring in urban areas. The proportion of paediatric asthma cases attributable to NO_2 in urban areas decreased from 19.8% in 2000 to 16.0% in 2019. Variations in the decline of urban attributable fractions were observed across different regions, with decreases in high-income countries, Latin America and the Caribbean, central Europe, eastern Europe, central Asia, southeast Asia, east Asia, and Oceania, and increases in south Asia, sub-Saharan Africa, and north Africa and the Middle East. The changes in NO_2-attributable paediatric asthma rates were influenced by NO_2 concentrations, paediatric population size, and asthma incidence rates, which varied regionally (Anenberg *et al*., 2022). Zhao *et al.* (2021) also analysed respiratory impacts in children by analysing data from 915 children within the GINIplus and LISA birth cohorts from Munich (n = 181) and Wesel (n = 734) Germany. They found that per interquartile range increase in air pollutants during the first year of life, forced expiratory volume in one second (FEV1) z-scores declined annually by -0.012 for $PM_{2.5}$ to -0.023 for the PMcoarse fraction[3]. Effect estimates of infancy exposure for certain air pollutants were higher for groups with asthma, older maternal age, and breastfeeding <12 weeks than their counterparts. These results indicate that infancy exposure to higher air pollution may reduce lung function development up to adolescence (15 years) (Q. Zhao *et al*., 2021). The studies conducted by Anenberg *et al.* (2022) and Zhao *et al.* (2021) provide valuable insights into the detrimental effects of air pollution on

[3] The coarse fraction contains the larger particles with a size ranging from 2.5 to 10 µm (PM_{10} - $PM_{2.5}$).

paediatric respiratory health, adding to the large consensus identified in the Dominski review.

Soarez and Silva (2022) reviewed the effects of ground-level O_3 on respiratory health. They identified 59 eligible studies, of which 83% presented significant correlations between O_3 with asthma, COPD, or acute respiratory distress syndrome (ARDS). The eligible studies that reported negative non-significant associations discussed a lack of data or topographic differences as the main issue with these divergent results (Soares and Silva, 2022).

It is widely accepted that air pollution may have harmful effects on pre-existing respiratory conditions. One study aimed to investigate personal exposure to air pollution and its effects on the respiratory health of COPD patients in London. A small number of patients (n=115) carried a personal monitor specifically designed to measure temperature, NO_2, O_3, NO, CO, $PM_{2.5}$ and PM_{10}. Individuals also recorded daily information on respiratory symptoms and measured peak expiratory flow (They found that gaseous air pollutants were associated with a deterioration in COPD patients' health. They observed an increase of 16.4%, 9.4% and 7.6% in the odds of exacerbation for an interquartile range increase in NO_2, NO and CO, respectively. O_3 was observed to have adverse associations with peak expiratory flow and breathlessness. No association was observed between particulate matter and any outcome (Evangelopoulos *et al*., 2021). This evidence highlights the importance of considering the effects of air pollution on respiratory health for both individuals with diagnosed conditions, as well as those who may develop health outcomes due to exposure.

In conclusion, the Dominski review provided a strong evidence base for the harmful effects of air pollution on respiratory health. The studies reviewed here are consistent with previous findings. This evidence highlights the need for comprehensive measures to mitigate air pollution and protect respiratory health, considering both pre-existing conditions and potential future health risks for individuals exposed to pollutants.

4.3.7 Development

As discussed, the harmful effects of air pollution on cognition were observed in studies looking at prenatal exposure (Zhang *et al*., 2022). In addition, prenatal exposure to air pollution has been associated with harmful effects on a child's neuropsychological functioning. Iglesias-Vasquez *et al.* (2022) analysed and modelled data from 473 mother-child pairs within the ECLIPSES study in Catalonia, Spain. Their model, once adjusted for maternal biological, sociodemographic and lifestyle characteristics, area deprivation index, and amount of greenness around the home's address, showed that all air pollutants assessed, except $PM_{2.5}$ absorbance, were associated with lower motor function in children, although no association between prenatal exposure to air pollution and cognitive and language functions was observed (Iglesias-Vázquez *et al*., 2022).

However, not all research on pre-natal air pollution has found evidence of harmful associations. Starling *et al.* (2022) calculated the average $PM_{2.5}$ and O_3 in each trimester of pregnancy to estimate the effects on DNA methylation detectable at birth. Whilst some differentially methylated regions were identified, no statistically significant associations were observed (Starling *et al*., 2022).

In addition to prenatal exposure, there is evidence for the harmful effects of air pollution exposure during early life and childhood. Ahmed *et al.* (2022) used data from the Mothers and their Children's Health (MatCH) study, a 2016/17 sub-study from a prospective longitudinal study, the Australian Longitudinal Study on Women's Health, and found that children who were exposed to moderate and high levels of $PM_{2.5}$ had higher odds of emotional and behavioural problems, and gross motor delay, compared with children with low levels of exposure. Children's lifetime exposure to 'moderate levels' of $PM_{2.5}$ (5.9–7.1 μg/m^3) was associated with 1.27-fold higher odds of emotional/behavioural problems. There was not enough evidence to demonstrate an association between NO_2 exposure or living within 200 m of major roads (Ahmed *et al*., 2022).

In conclusion, the effects of prenatal exposure to air pollution on prenatal and childhood development presented in these studies is inconclusive and more comprehensive studies are needed to better understand the complex relationship.

4.3.8 Mortality

Three studies investigated the association between air pollution and mortality. Bai *et al.* (2022) investigated the relationship between outdoor $PM_{2.5}$ exposure and mortality. Their analysis showed that every 10 μg/m^3 increase in $PM_{2.5}$ is associated with approximately two deaths, of which 31.7% were attributable to diabetes and major cardiovascular events. Specifically, 4.5% were explained by $PM_{2.5}$-induced diabetes, 22.8% by $PM_{2.5}$-induced major cardiovascular events, and 4.5% through their interaction (Bai *et al*., 2022). A large Danish study analysed data from over 3 million residents aged 30 or older from 2000 to 2017, alongside estimated annual mean concentrations of $PM_{2.5}$, NO_2, BC and O_3. Their findings showed that long-term exposure to $PM_{2.5}$, NO_2 and/or BC was significantly associated with mortality from various causes. An increase of 5 μg/m^3 in $PM_{2.5}$ was associated with higher mortality rates for all-natural causes, cardiovascular disease, respiratory disease, lung cancer, diabetes, dementia, psychiatric disorders, asthma, and acute lower respiratory infection. The associations with long-term exposure to O_3 were generally negative, meaning the more O_3 the less harmful effects on health. The study's results remained significant even after adjusting for demographic and socioeconomic factors, as well as indirect adjustment for smoking and body mass index (So *et al*., 2022).

So *et al.* (2023) also used this data set to evaluate the associations between mortality and long-term exposure to eight $PM_{2.5}$ elemental components (copper, iron, zinc, sulphur, nickel, vanadium, silicon, and potassium). Their analysis found significant positive associations between all-natural mortality with silicon and potassium with most causes of mortality, excluding chronic kidney disease and potassium, and diabetes and silicon. The strongest associations were for psychiatric disorder mortality and in addition, iron was relevant for mortality from respiratory diseases, lung cancer, chronic kidney disease, and psychiatric disorders; zinc with mortality from chronic kidney disease, respiratory disease, and lung cancer, and nickel and vanadium with lung cancer mortality (So *et al*., 2023).

In conclusion, the three studies provide evidence for the association between air pollution and mortality. Bai *et al.* (2022) found a significant relationship between $PM_{2.5}$ exposure and mortality, with a substantial proportion of deaths attributable to diabetes and major cardiovascular events. The Danish study by So *et al*. (2022) revealed that long-term exposure to $PM_{2.5}$, NO_2, and BC was associated with increased mortality from various causes, while O_3 showed a generally negative association. Furthermore, So *et al*. (2023) identified significant positive associations between mortality and exposure to specific $PM_{2.5}$ elemental components. These findings highlight the adverse health effects of air pollution on mortality, in addition to the specific health outcomes discussed in this report.

4.3.9 Cancer

The Dominski review identified two papers assessing the relationship between air pollution and cancer and a relative lack of literature in comparison to other health outcomes. Additionally, the review identified no evidence associating air pollution and childhood cancer. However, the two papers identified demonstrated an association between $PM_{2.5}$ and PM_{10} and breast cancer mortality; namely each 10 µg/m^3 of $PM_{2.5}$ was associated with 1.17-fold increase in risk and each 10 µg/m^3 of PM_{10} was associated with 1.1-fold increased risk (Dominski *et al*., 2021). The search conducted in this report identified two additional papers focusing on the association between cancer and air pollution, both of which demonstrated a positive association. Yim *et al.* (2022) analysed global trends in lung cancer incidence over a 22-year period, from 1990 to 2012, and investigated the association between air pollution and lung cancer rates alongside the risk from smoking. Their analysis shows that the global decrease in lung squamous cell carcinoma incidence is associated with reduced tobacco consumption whereas the increase in lung adenocarcinoma incidence is associated with air pollution. More specifically there is evidence of the potential involvement of black carbon and sulphate in the pathogenesis of lung adenocarcinoma (Yim *et al*., 2022).

Interestingly, whist the Dominski review found no evidence of synthesis reviews that analysed the association between air pollution and childhood cancer, Huls *et al.* (2023) analysed the environmental, social and behavioural risk factors associated with spatial clustering of childhood cancer incidence across 159 counties in Georgia (USA). Their analysis demonstrated consistent associations of environmental (pesticide exposure) and social/behavioural stressors (low socioeconomic status, alcohol) with spatial clustering of paediatric cancer class II (lymphomas and reticuloendothelial neoplasms), but not for other cancer classes. Whilst an association between childhood cancers was demonstrated in the analysis, a direct link with air pollution was not established, as the environmental data on air pollution was clustered with other environmental risk factors (Hüls *et al*., 2023).

The association between air pollution and cancers is evidenced in the literature, however the strength of the association is not as well established as it is for other health outcomes. Furthermore, the relationship more specifically with childhood cancers has limited evidence and needs further assessment.

4.3.10 Neonatal

Recent research has begun to consider the effects of air pollution during neonatal development. Ren *et al.* (2023) investigated the spatiotemporal changes in neonatal disease burden caused by $PM_{2.5}$ at a global level, considering the socio-demographic index (SDI), gender and nationality. Using data from the Global Burden of Disease Study database, they found that the burden of neonatal diseases associated with $PM_{2.5}$ has increased since 1990, particularly in regions with lower SDI, such as South Asia and Sub-Saharan Africa. Neonatal preterm birth was identified as the leading cause of preterm death. The global age-standardized mortality rate was 2.09 per 100,000 population in 2019. The study highlights $PM_{2.5}$ as a significant environmental hazard for new-born diseases (Ren *et al.*, 2023). Zhao *et al.* (2023) also used the Global Burden of Disease Study database to examine the spatiotemporal trends in the burden of neonatal disorders caused by ambient and household $PM_{2.5}$ at global, regional, and national levels from 1990 to 2019. In 2019, approximately one-fifth of global neonatal disorders was attributed to $PM_{2.5}$ exposure, with ambient $PM_{2.5}$ accounting for 7.5% and household $PM_{2.5}$ for 13.2%. The burden of neonatal disorders related to household $PM_{2.5}$ decreased between 1990 and 2019, while that related to ambient $PM_{2.5}$ increased, particularly in regions with lower SDI. South Asia and East Asia had the highest rates and population attributable fractions (PAFs) of ambient $PM_{2.5}$-related neonatal disorders DALYs in 2019. There was an inverted V-shaped relationship between rates and population PAFs of ambient $PM_{2.5}$-related neonatal disorders DALYs in 2019, as well as their corresponding estimated annual percentage change (EAPCs), with SDI, whereas rates and PAFs of household $PM_{2.5}$-related neonatal disorders DALYs in 2019 showed a highly negative correlation with SDI. Overall, the burden of ambient $PM_{2.5}$-related neonatal disorders has significantly increased over the past three decades, particularly in regions with lower SDI, while household $PM_{2.5}$-related burden has decreased but still represents a substantial portion of the overall burden of $PM_{2.5}$-related neonatal diseases (Zhao *et al.*, 2023).

In conclusion, recent studies have shed light on the concerning impact of air pollution, particularly $PM_{2.5}$, on neonatal health, however further evidence is needed to understand the extent of this impact and the underlying biological mechanisms.

4.3.11 Type-2 Diabetes

Air pollution has emerged as a significant environmental risk factor associated with various health conditions, including type-2 diabetes. A systematic review and meta-analysis by Yang *et al.* (2020) compiled the evidence showing significant associations of $PM_{2.5}$, PM_{10} and NO_2 with type-2 diabetes incidence and prevalence. Also, whilst the data was too heterogeneous for meta-analysis the majority of studies on glucose-homoeostasis markers also showed increased risks with higher air pollutants levels (Yang *et al.*, 2020). Liu *et al.* (2021) evaluated the spatio-temporal changes in type-2 diabetes incidence and prevalence attributed to $PM_{2.5}$ from 1990 to 2019 in 204 countries and regions. Their analysis found that overall the global burden of type-2 diabetes attributable to $PM_{2.5}$ increased significantly since 1990, particularly within specific demographic groups including the elderly, males, as well as individuals living in Africa, Asia and low-middle SDI regions (Liu *et al*., 2021). However, declining trends were observed in North America, South America, Europe, Australia, and other regions with high SDI. Bai *et al.* (2022) investigated the relationship between outdoor $PM_{2.5}$ exposure and mortality. Of over 200,000 individuals analysed in Ontario, Canada, from 1996 to 2014, they estimated that each 10 μg/m^3 increase in $PM_{2.5}$ was associated with approximately two incident cases of diabetes. Further to this, every 10 μg/m^3 increase in $PM_{2.5}$ is associated with approximately two deaths, of which 31.7% were attributable to diabetes and major cardiovascular events. Specifically, 4.5% were explained by $PM_{2.5}$-induced diabetes, 22.8% by $PM_{2.5}$-induced major cardiovascular events, and 4.5% through their interaction (Bai *et al*., 2022).

The Dominski review, as well as the evidence discussed, supports a significant association between air pollution, specifically $PM_{2.5}$, and the incidence and prevalence of type-2 diabetes.

4.3.12 Ocular

Only one study from the search analysed the effects of air pollution on ocular outcomes such as visual impairment and age-related eye disease. This study utilised data from the Canadian Longitudinal Study on Aging, including 30,097 adults aged 45 to 85 years, alongside annual mean $PM_{2.5}$ data estimated from satellite data to residents' home address. The analysis showed that increased $PM_{2.5}$ levels were associated with visual impairment, glaucoma, and visually impairing age-related macular degeneration. In the single pollutant models, increased $PM_{2.5}$ levels (per interquartile range) were associated with visual impairment (odds ratio [OR] = 1.12), glaucoma (OR = 1.14), and visually impairing age-related macular degeneration (OR = 1.52) after adjustment for sociodemographic variables and co-morbidities. There was also limited evidence of a week association (after adjustment) with cataract (OR = 1.06). Whilst based upon one study, there is an observed associations between $PM_{2.5}$ and ocular outcomes, suggesting the need for further studies to confirm these associations and explore potential mechanisms (Grant et al., 2021).

4.3.13 Primary care healthcare service use

One study analysed the effects of air pollution on short term primary and pharmaceutical care usage. Following several mine fires between February and March 2014 births, general practitioner (GP) presentations and prescription dispensing for children born in the Latrobe Valley, Australia. They observed that exposure to fire related $PM_{2.5}$ during pregnancy was associated with an increase in the dispensing of systemic steroids, while exposure during infancy was linked to antibiotic dispensing. Additionally, even at relatively low levels, exposure to ambient $PM_{2.5}$ during infancy was associated with an increase in antibiotics and GP presentations, independent of exposure to the fire. Sex-specific differences were observed, with stronger associations in girls for GP presentations and stronger associations in boys for steroid skin cream dispensing. These findings highlight the potential health effects of $PM_{2.5}$ exposure during critical developmental periods and the importance of considering sex differences in susceptibility (Ziou *et al*., 2023).

4.3.14 Contradictory evidence

This report identified two studies (Cortes *et al.* 2023; Kusters *et al.* 2022) which did not report any positive association between air pollution and the studies' health outcome.

Firstly, Cortes *et al.* (2023) used a time-stratified case-crossover study design with individual-level mortality data to estimate the short-term association between exposure to PM_{10} and O_3, and cardiovascular and respiratory mortality in Rio de Janeiro, Brazil, between 2012 and 2017. They observed no consistent associations between pollutant and mortality outcomes. However, this study has several limitations that should be considered. Firstly, the study relies on an ecological design, which can limit causal inferences at the individual level. Secondly, the analysis only considers two pollutants and does not account for potential confounding factors such as socio-economic status, smoking prevalence, or access to healthcare. These factors could therefore explain the absence of observed associations.

Secondly, Kusters *et al.* (2022) examined the association between exposure to air pollution during pregnancy and childhood and cognitive function, as well as emotional and behavioural problems, in adolescents. They analysed data from a birth cohort in Rotterdam (n=5,170). Air pollutant concentrations were estimated using land use regression models. Various cognitive domains and emotional and behavioural problems were assessed through self- and parent-reported measures. There was no observed association between air pollution exposure during pregnancy and childhood and lower cognitive function, or an increased prevalence of emotional and behavioural problems in adolescents. However, the authors recognise that the absence of any observed associations was likely due to factors such as residual confounding, selection bias, or chance, and that further research is needed to understand if a causal relationship may exist.

These studies do not negate the level of evidence for the negative health impacts of air pollution; however, they do highlight the need for further research using more robust methodologies and comprehensive confounding adjustments to better understand the complex relationship between air pollution and health outcomes and importantly the best way of evaluating the associations and potential causality.

5 Conclusion

The Scottish Government commissioned a comprehensive review to examine the existing evidence on the health effects associated with low-level pollution in countries that have levels of ambient air pollution similar to Scotland. We conducted a robust, rapid evidence review focusing on the most recent publications since 1 January 2022 to complement the findings from supplementary searches which identified key literature, including the Dominski review and the three HEI reports.

The evidence identified in this review primarily focused on mental health and well-being, cognition, and dementia. However, it should be noted that this emphasis is likely an artefact of the review's temporal scope (2020 onwards), as the literature has extensively documented other health effects including CVD, respiratory and cancers for many years. Furthermore, this review considered the inconclusive evidence from Scotland regarding the association of air pollution with cardiovascular disease, as well as the potential contributing factors to this variation.

In conclusion, the evidence from global studies and reviews consistently supports the association between air pollution and various health outcomes, including CVD, respiratory health, mortality, cancer, neonatal health, type-2 diabetes, ocular outcomes, primary care healthcare service use, cognition, and neurological health. The studies also highlight the association between air pollution and mental health, including self-harm, psychopathology, major depressive disorder, and cognitive impairments. Furthermore, air pollution contributes to the development and exacerbation of dementias and is associated with neurological diseases such as Parkinson's disease, stroke, multiple sclerosis, and nervous system disorders.

While the global evidence is robust, the specific evidence regarding air pollution and health outcomes in Scotland is limited and inconclusive. When specifically considering CVD, some studies in Scottish cohorts support the global consensus, showing associations between air pollution and CVD, while others did not find significant associations, possibly due to methodological limitations and challenges in adjusting for confounding factors. Further research in the Scottish context, considering multiple pollutants and addressing data limitations, is necessary to provide more conclusive insights into the relationship between air pollution and health outcomes in Scotland.

Overall, the Dominski review, three HEI reports and recent evidence identified and discussed in this review emphasis the broad range of impacts from air pollution and the necessity to mitigate the harmful health effects of air pollution, promoting public health and well-being. As these harmful effects have been extensively evidenced at concentrations below national and international air quality standards, effective policies and interventions are necessary to reduce air pollution levels. In addition, further research is needed to better understand the underlying mechanisms behind these impacts and explore potential associations in specific health outcomes, allowing the development of prevention and targeted interventions in populations, particularly those most vulnerable.

References

Ahmed, S.M., Mishra, G.D., Moss, K.M., Yang, I.A., Lycett, K., Knibbs, L.D., 2022. Maternal and Childhood Ambient Air Pollution Exposure and Mental Health Symptoms and Psychomotor Development in Children: An Australian Population-Based Longitudinal Study. Environ. Int. 158, 107003. https://doi.org/10.1016/j.envint.2021.107003

Al Ahad, M.A., Demšar, U., Sullivan, F., Kulu, H., 2022. Does Long-Term Air Pollution Exposure Affect Self-Reported Health and Limiting Long Term Illness Disproportionately for Ethnic Minorities in the UK? A Census-Based Individual Level Analysis. Appl. Spat. Anal. Policy 15, 1557–1582. https://doi.org/10.1007/s12061-022-09471-1

Andersson, J., Sundström, A., Nordin, M., Segersson, D., Forsberg, B., Adolfsson, R., Oudin, A., 2023. PM 2.5 and Dementia in a Low Exposure Setting: The Influence of Odor Identification Ability and APOE. J. Alzheimers Dis. 92, 679–689. https://doi.org/10.3233/JAD-220469

Anenberg, S.C., Mohegh, A., Goldberg, D.L., Kerr, G.H., Brauer, M., Burkart, K., Hystad, P., Larkin, A., Wozniak, S., Lamsal, L., 2022. Long-term trends in urban NO2 concentrations and associated paediatric asthma incidence: estimates from global datasets. Lancet Planet. Health 6, e49–e58. https://doi.org/10.1016/S2542-5196(21)00255-2

Bai, L., Benmarhnia, T., Chen, C., Kwong, J.C., Burnett, R.T., van Donkelaar, A., Martin, R.V., Kim, J., Kaufman, J.S., Chen, H., 2022. Chronic Exposure to Fine Particulate Matter Increases Mortality Through Pathways of Metabolic and Cardiovascular Disease: Insights From a Large Mediation Analysis. J. Am. Heart Assoc. 11. https://doi.org/10.1161/JAHA.122.026660

Brauer, M., Brook, J.R., Christidis, T., Chu, Y., Crouse, D.L., Erickson, A., Hystad, P., Li, C., Martin, R.V., Meng, J., Pappin, J., Pinault, L.L., Tjepkema, M., van Donkelaar, A., Weichenthal, S., Burnett, R.T., 2022. Mortality–Air Pollution Associations in Low Exposure Environments (MAPLE): Phase 2.

Brunekreef, B., Strak, M., Chen, J., Andersen, Z.J., Atkinson, R., Carey, I., Cesaroni, G., Forastiere, F., Fecht, D., Gulliver, J., Hertel, O., Hoffmann, B., de Hoogh, K., Houthuijs, D., Hvidtfeldt, U., Klompmaker, J., Krog, N.H., Liu, S., Ljungman, P., Mehta, A., Renzi, M., Rodopoulou, S., Samoli, E., Schwarze, P., Sigsgaard, T., Stafoggia, M., Vienneau, D., Weinmayr, G., Wolf, K., Hoek, G., 2021. Mortality and Morbidity Effects of Long-Term Exposure to Low-Level PM2.5, BC, NO2, and O3: An Analysis of European Cohorts in the ELAPSE Project.

Carroll, M., Gao, C.X., Campbell, T.C.H., Smith, C.L., Dimitriadis, C., Berger, E., Maybery, D., Ikin, J., Abramson, M.J., Sim, M.R., McFarlane, A., Smith, K., Guo, Y., 2022. Impacts of coal mine fire-related PM2.5 on the utilisation of ambulance and hospital services for mental health conditions. Atmospheric Pollut. Res. 13, 101415. https://doi.org/10.1016/j.apr.2022.101415

Chastko, K. and Adams, M. (2019) Assessing the accuracy of long-term air pollution estimates produced with temporally adjusted short-term observations from unstructured sampling. *Journal of Environmental Management* [online]. 240, pp. 249–258.

Christensen, G.M., Li, Z., Pearce, J., Marcus, M., Lah, J.J., Waller, L.A., Ebelt, S., Hüls, A., 2022. The complex relationship of air pollution and neighborhood socioeconomic status and their association with cognitive decline. Environ. Int. 167, 107416. https://doi.org/10.1016/j.envint.2022.107416

Cortes, T.R., I.H. Silveira, B.F.A. de Oliveira, M.L. Bell, and W.L. Junger. 'Short-Term Association between Ambient Air Pollution and Cardio-Respiratory Mortality in Rio de Janeiro, Brazil'. *PLoS ONE* 18, no. 2 February (2023). https://doi.org/10.1371/journal.pone.0281499.

Dominici, F., Zanobetti, A., Schwartz, J., Braun, D., Sabath, B., Wu, X., 2019. Assessing Adverse Health Effects of Long- Term Exposure to Low Levels of Ambient Air Pollution: Implementation of Causal Inference Methods.

Dominski, F.H., Lorenzetti Branco, J.H., Buonanno, G., Stabile, L., Gameiro da Silva, M., Andrade, A., 2021. Effects of air pollution on health: A mapping review of systematic reviews and meta-analyses. Environ. Res. 201, 111487. https://doi.org/10.1016/j.envres.2021.111487

Evangelopoulos, D., Chatzidiakou, L., Walton, H., Katsouyanni, K., Kelly, F.J., Quint, J.K., Jones, R.L., Barratt, B., 2021. Personal exposure to air pollution and respiratory health of COPD patients in London. Eur. Respir. J. 58. https://doi.org/10.1183/13993003.03432-2020

Goria, S., Pascal, M., Corso, M., Le Tertre, A., 2021. Short-term exposure to air pollutants increases the risk of hospital admissions in patients with Parkinson's disease – A multicentric study on 18 French areas. Atmos. Environ. 264. https://doi.org/10.1016/j.atmosenv.2021.118668

Grant, A., Leung, G., Aubin, M.-J., Kergoat, M.-J., Li, G., Freeman, E.E., 2021. Fine Particulate Matter and Age-Related Eye Disease: The Canadian Longitudinal Study on Aging. Invest. Ophthalmol. Vis. Sci. 62, 7. https://doi.org/10.1167/iovs.62.10.7

Health Effects Institute. 2020. State of Global Air 2020. Data source: Global Burden of Disease Study 2019. IHME, 2020. https://www.stateofglobalair.org/data/#/air/table

Health Effects Institute, 2014. 14-3 Assessing Health Effects of Long-term Exposure to Low Levels of Ambient Air Pollution [WWW Document]. Health Eff. Inst. URL https://www.healtheffects.org/research/funding/rfa/14-3-assessing-health-effects-long-term-exposure-low-levels-ambient-air-pollution (accessed 4.14.23).

Hüls, A., Van Cor, S., Christensen, G.M., Li, Z., Liu, Y., Shi, L., Pearce, J.L., Bayakly, R., Lash, T.L., Ward, K., Switchenko, J.M., 2023. Environmental, social and behavioral risk factors in association with spatial clustering of childhood cancer incidence. Spat. Spatio-Temporal Epidemiol. 45, 100582. https://doi.org/10.1016/j.sste.2023.100582

Iglesias-Vázquez, L., Binter, A.-C., Canals, J., Hernández-Martínez, C., Voltas, N., Ambròs, A., Fernández-Barrés, S., Pérez-Crespo, L., Guxens, M., Arija, V., 2022. Maternal exposure to air pollution during pregnancy and child's cognitive, language, and motor function: ECLIPSES study. Environ. Res. 212, 113501. https://doi.org/10.1016/j.envres.2022.113501

Kriit, H.K., B. Forsberg, D.O. Åström, and A. Oudin. 'Annual Dementia Incidence and Monetary Burden Attributable to Fine Particulate Matter (PM2.5) Exposure in Sweden'. *Environmental Health: A Global Access Science Source* 20, no. 1 (2021). https://doi.org/10.1186/s12940-021-00750-x.

Kusters, M.S.W., E. Essers, R. Muetzel, A. Ambrós, H. Tiemeier, and M. Guxens. 'Air Pollution Exposure during Pregnancy and Childhood, Cognitive Function, and Emotional and Behavioral Problems in Adolescents'. Environmental Research 214 (2022). https://doi.org/10.1016/j.envres.2022.113891.

Latham, R.M., Kieling, C., Arseneault, L., Botter-Maio Rocha, T., Beddows, A., Beevers, S.D., Danese, A., De Oliveira, K., Kohrt, B.A., Moffitt, T.E., Mondelli, V., Newbury, J.B., Reuben, A., Fisher, H.L., 2021. Childhood exposure to ambient air pollution and predicting individual risk of depression onset in UK adolescents. J. Psychiatr. Res. 138, 60–67. https://doi.org/10.1016/j.jpsychires.2021.03.042

Lee, D., Robertson, C., Ramsay, C., Gillespie, C., Napier, G., 2019. Estimating the health impact of air pollution in Scotland, and the resulting benefits of reducing concentrations in city centres. Spat. Spatio-Temporal Epidemiol. 29, 85–96. https://doi.org/10.1016/j.sste.2019.02.003

Li, D., Xie, J., Wang, L., Sun, Y., Hu, Y., Tian, Y., 2023. Genetic susceptibility and lifestyle modify the association of long-term air pollution exposure on major depressive disorder: a prospective study in UK Biobank. BMC Med. 21, 67. https://doi.org/10.1186/s12916-023-02783-0

Li, Y., Xie, T., Cardoso Melo, R.D., de Vries, M., Lakerveld, J., Zijlema, W., Hartman, C.A., 2023. Longitudinal effects of environmental noise and air pollution exposure on autism spectrum disorder and attention-deficit/hyperactivity disorder during adolescence and early adulthood: The TRAILS study. Environ. Res. 227, 115704. https://doi.org/10.1016/j.envres.2023.115704

Liu, C., Wang, B., Liu, S., Li, S., Zhang, K., Luo, B., Yang, A., 2021. Type 2 diabetes attributable to PM2.5: A global burden study from 1990 to 2019. Environ. Int. 156, 106725. https://doi.org/10.1016/j.envint.2021.106725

Lukina, A.O., Burstein, B., Szyszkowicz, M., 2022. Urban air pollution and emergency department visits related to central nervous system diseases. PLOS ONE 17, e0270459. https://doi.org/10.1371/journal.pone.0270459

Min, J., Lee, W., Bell, M.L., Kim, Y., Heo, S., Kim, G.E., Kim, J.H., Yun, J.Y., Kim, S.I., Schwartz, J., Ha, E., 2023. Hospital admission risks and excess costs for neurological symptoms attributable to long-term exposure to fine particulate matter in New York State, USA. Environ. Res. 229, 115954. https://doi.org/10.1016/j.envres.2023.115954

Mok, P.L.H., Antonsen, S., Agerbo, E., Brandt, J., Geels, C., Christensen, J.H., Frohn, L.M., Pedersen, C.B., Webb, R.T., 2021. Exposure to ambient air pollution during childhood and subsequent risk of self-harm: A national cohort study. Prev. Med. 152, 106502. https://doi.org/10.1016/j.ypmed.2021.106502

Mortamais, M., Gutierrez, L.-A., de Hoogh, K., Chen, J., Vienneau, D., Carrière, I., Letellier, N., Helmer, C., Gabelle, A., Mura, T., Sunyer, J., Benmarhnia, T., Jacquemin, B., Berr, C., 2021. Long-term exposure to ambient air pollution and risk of dementia: Results of the prospective Three-City Study. Environ. Int. 148, 106376. https://doi.org/10.1016/j.envint.2020.106376

Muhsin, H.A., Steingrimsson, S., Oudin, A., Åström, D.O., Carlsen, H.K., 2022. Air pollution and increased number of psychiatric emergency room visits: A case-crossover study for identifying susceptible groups. Environ. Res. 204, 112001. https://doi.org/10.1016/j.envres.2021.112001

Newbury, J.B., Arseneault, L., Caspi, A., Moffitt, T.E., Odgers, C.L., Belsky, D.W., Sugden, K., Williams, B., Ambler, A.P., Matthews, T., Fisher, H.L., 2022. Association between genetic and socioenvironmental risk for schizophrenia during upbringing in a UK longitudinal cohort. Psychol. Med. 52, 1527–1537. https://doi.org/10.1017/S0033291720003347

Parra, K.L., Alexander, G.E., Raichlen, D.A., Klimentidis, Y.C., Furlong, M.A., 2022. Exposure to air pollution and risk of incident dementia in the UK Biobank. Environ. Res. 209, 112895. https://doi.org/10.1016/j.envres.2022.112895

Petrowski, K., Bührer, S., Strauß, B., Decker, O., Brähler, E., 2021. Examining air pollution (PM10), mental health and well-being in a representative German sample. Sci. Rep. 11. https://doi.org/10.1038/s41598-021-93773-w

Qiu, X., Danesh-Yazdi, M., Wei, Y., Di, Q., Just, A., Zanobetti, A., Weisskopf, M., Dominici, F., Schwartz, J., 2022. Associations of short-term exposure to air pollution and increased ambient temperature with psychiatric hospital admissions in older adults in the USA: a case–crossover study. Lancet Planet. Health 6, e331–e341. https://doi.org/10.1016/S2542-5196(22)00017-1

Ren, B., He, Q., Ma, J., Zhang, G., 2023. A preliminary analysis of global neonatal disorders burden attributable to PM2.5 from 1990 to 2019. Sci. Total Environ. 870, 161608. https://doi.org/10.1016/j.scitotenv.2023.161608

Reuben, A., Arseneault, L., Beddows, A., Beevers, S.D., Moffitt, T.E., Ambler, A., Latham, R.M., Newbury, J.B., Odgers, C.L., Schaefer, J.D., Fisher, H.L., 2021. Association of Air Pollution Exposure in Childhood and Adolescence with Psychopathology at the Transition to Adulthood. JAMA Netw. Open 4. https://doi.org/10.1001/jamanetworkopen.2021.7508

So, R., Andersen, Z.J., Chen, J., Stafoggia, M., de Hoogh, K., Katsouyanni, K., Vienneau, D., Rodopoulou, S., Samoli, E., Lim, Y.-H., Jørgensen, J.T., Amini, H., Cole-Hunter, T., Mahmood

Taghavi Shahri, S., Maric, M., Bergmann, M., Liu, S., Azam, S., Loft, S., Westendorp, R.G.J., Mortensen, L.H., Bauwelinck, M., Klompmaker, J.O., Atkinson, R., Janssen, N.A.H., Oftedal, B., Renzi, M., Forastiere, F., Strak, M., Thygesen, L.C., Brunekreef, B., Hoek, G., Mehta, A.J., 2022. Long-term exposure to air pollution and mortality in a Danish nationwide administrative cohort study: Beyond mortality from cardiopulmonary disease and lung cancer. Environ. Int. 164, 107241. https://doi.org/10.1016/j.envint.2022.107241

So, R., Chen, J., Stafoggia, M., de Hoogh, K., Katsouyanni, K., Vienneau, D., Samoli, E., Rodopoulou, S., Loft, S., Lim, Y.-H., Westendorp, R.G.J., Amini, H., Cole-Hunter, T., Bergmann, M., Shahri, S.M.T., Zhang, J., Maric, M., Mortensen, L.H., Bauwelinck, M., Klompmaker, J.O., Atkinson, R.W., Janssen, N.A.H., Oftedal, B., Renzi, M., Forastiere, F., Strak, M., Brunekreef, B., Hoek, G., Andersen, Z.J., 2023. Long-term exposure to elemental components of fine particulate matter and all-natural and cause-specific mortality in a Danish nationwide administrative cohort study. Environ. Res. 224, 115552. https://doi.org/10.1016/j.envres.2023.115552

Soares, A.R., Silva, C., 2022. Review of Ground-Level Ozone Impact in Respiratory Health Deterioration for the Past Two Decades. Atmosphere 13, 434. https://doi.org/10.3390/atmos13030434

Starling, A.P., Wood, C., Liu, C., Kechris, K., Yang, I.V., Friedman, C., Thomas, D.S.K., Peel, J.L., Adgate, J.L., Magzamen, S., Martenies, S.E., Allshouse, W.B., Dabelea, D., 2022. Ambient air pollution during pregnancy and DNA methylation in umbilical cord blood, with potential mediation of associations with infant adiposity: The Healthy Start study. Environ. Res. 214. https://doi.org/10.1016/j.envres.2022.113881

The Air Quality Standards Regulations 2010 [WWW Document], n.d. URL https://www.legislation.gov.uk/uksi/2010/1001/contents/made (accessed 7.7.23).

Thompson, R., Smith, R.B., Karim, Y.B., Shen, C., Drummond, K., Teng, C., Toledano, M.B., 2023. Air pollution and human cognition: A systematic review and meta-analysis. Sci. Total Environ. 859, 160234. https://doi.org/10.1016/j.scitotenv.2022.160234

UKHSA, 2022. Statement on the differential toxicity of particulate matter according to source or constituents: 2022 [WWW Document]. GOV.UK. URL https://www.gov.uk/government/publications/particulate-air-pollution-health-effects-of-exposure/statement-on-the-differential-toxicity-of-particulate-matter-according-to-source-or-constituents-2022 (accessed 6.22.23).

Wang, Y., Crowe, M., Knibbs, L.D., Fuller-Tyszkiewicz, M., Mygind, L., Kerr, J.A., Wake, M., Olsson, C.A., Enticott, P.G., Peters, R.L., Daraganova, G., Mavoa, S., Lycett, K., 2023. Greenness modifies the association between ambient air pollution and cognitive function in Australian adolescents, but not in mid-life adults. Environ. Pollut. 324, 121329. https://doi.org/10.1016/j.envpol.2023.121329

Willocks, L.J., Bhaskar, A., Ramsay, C.N., Lee, D., Brewster, D.H., Fischbacher, C.M., Chalmers, J., Morris, G., Scott, E.M., 2012. Cardiovascular disease and air pollution in

Scotland: no association or insufficient data and study design? BMC Public Health 12, 227. https://doi.org/10.1186/1471-2458-12-227

Wu, J., Grande, G., Stafoggia, M., Ljungman, P., Laukka, E.J., Eneroth, K., Bellander, T., Rizzuto, D., 2022. Air pollution as a risk factor for Cognitive Impairment no Dementia (CIND) and its progression to dementia: A longitudinal study. Environ. Int. 160. https://doi.org/10.1016/j.envint.2021.107067

Yang, B.-Y., Fan, S., Thiering, E., Seissler, J., Nowak, D., Dong, G.-H., Heinrich, J., 2020. Ambient air pollution and diabetes: A systematic review and meta-analysis. Environ. Res. 180, 108817. https://doi.org/10.1016/j.envres.2019.108817

Yap, Christina, Iain J. Beverland, Mathew R. Heal, Geoffrey R. Cohen, Chris Robertson, Deborah E. J. Henderson, Neil S. Ferguson, Carole L. Hart, George Morris, and Raymond M. Agius. 'Association between Long-Term Exposure to Air Pollution and Specific Causes of Mortality in Scotland'. *Occupational and Environmental Medicine* 69, no. 12 (1 December 2012): 916–24. https://doi.org/10.1136/oemed-2011-100600.

Yim, S.H.L., Huang, T., Ho, J.M.W., Lam, A.S.M., Yau, S.T.Y., Yuen, T.W.H., Dong, G.H., Tsoi, K.K.F., Sung, J.J.Y., 2022. Rise and fall of lung cancers in relation to tobacco smoking and air pollution: A global trend analysis from 1990 to 2012. Atmos. Environ. 269, 118835. https://doi.org/10.1016/j.atmosenv.2021.118835

Zhang, X., Liu, S.H., Geron, M., Mathilda Chiu, Y.-H., Gershon, R., Ho, E., Huddleston, K., Just, A.C., Kloog, I., Coull, B.A., Enlow, M.B., Wright, R.O., Wright, R.J., 2022. Prenatal exposure to PM2.5 and childhood cognition: Accounting for between-site heterogeneity in a pooled analysis of ECHO cohorts in the Northeastern United States. Environ. Res. 214. https://doi.org/10.1016/j.envres.2022.114163

Zhao, H., Zhang, X., Wang, W., Shi, J., Lai, W., Li, Y., Zhang, C., Guo, L., Gong, J., Li, L., Lu, C., 2023. Global, regional, and national burden of ambient and household PM2.5-related neonatal disorders, 1990–2019. Ecotoxicol. Environ. Saf. 252, 114560. https://doi.org/10.1016/j.ecoenv.2023.114560

Zhao, N., Pinault, L., Toyib, O., Vanos, J., Tjepkema, M., Cakmak, S., 2021. Long-term ozone exposure and mortality from neurological diseases in Canada. Environ. Int. 157, 106817. https://doi.org/10.1016/j.envint.2021.106817

Zhao, Q., Kress, S., Markevych, I., Berdel, D., von Berg, A., Gappa, M., Koletzko, S., Bauer, C.-P., Schulz, H., Standl, M., Heinrich, J., Schikowski, T., 2021. Air pollution during infancy and lung function development into adolescence: The GINIplus/LISA birth cohorts study. Environ. Int. 146, 106195. https://doi.org/10.1016/j.envint.2020.106195

Ziou, M., Gao, C.X., Wheeler, A.J., Zosky, G.R., Stephens, N., Knibbs, L.D., Williamson, G.J., Melody, S.M., Venn, A.J., Dalton, M.F., Dharmage, S.C., Johnston, F.H., 2023. Primary and pharmaceutical care usage concurrent associations with a severe smoke episode and low ambient air pollution in early life. Sci. Total Environ. 883, 163580. https://doi.org/10.1016/j.scitotenv.2023.163580

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The Scottish Government
St Andrew's House
Edinburgh
EH1 3DG

ISBN: 978-1-83521-487-9 (web only)

Published by The Scottish Government, October 2023

Produced for The Scottish Government by APS Group Scotland, 21 Tennant Street, Edinburgh EH6 5NA
PPDAS1370314 (10/23)