

Health impact assessment of current and past air pollution on asthma in London

Independent analysis provided by:

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Peter Zheng undertook literature searching and sifting, Sofia Zafeiratou and Konstantina Dimakopoulou performed the meta-analyses and Shawn Lee assisted with the references.

Signed by Dr Heather Walton

28th February 2022

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1. Executive Summary and Key results

Previous studies have shown that numbers of asthma admissions are higher on days when pollution is higher. This report uses those previous studies to provide a modelled estimate of the impact of air pollution in London on asthma admissions, both at levels of pollution in 2019 and, for comparison, at levels of pollution in 2016 using the same methods.

Methodology

These estimates are obtained by combining the pollution concentrations in London with information from previous studies on the percentage change in asthma admissions on days with different air pollution concentrations. This percentage increase is then applied to the baseline numbers of asthma admissions in London. More specifically, the inputs were:

- Annual means¹ of 24-hour average fine particulate matter (PM_{2.5}) and nitrogen dioxide (NO₂) modelled at a 20x20m scale using the 2019 London Atmospheric Emissions Inventory (LAEI2019) with sea salt subtracted from PM_{2.5} to represent anthropogenic PM_{2.5}. These annual means were then averaged by Census Output Area (COA) and the population-weighting was done at Ward level (~13,000 residents). Ward level concentrations varied from 9.0 to 13.8 μg m⁻³ and from 18.2 to 42.1 μg m⁻³, for anthropogenic PM_{2.5} and NO₂, respectively.
- Percentage change in admissions per 10 μg m⁻³ change of pollutant concentration was derived by pooling the results of previous studies as part of this project. The chosen concentration response functions suggested percentage changes in admissions ranging from 1.2 to 3.9% per 10 μg m⁻³ increase depending on pollutant, age group and health outcome (chronic obstructive pulmonary disease (COPD) and asthma admissions combined were used for the elderly).
- Previous studies used to define the concentration-response functions were from locations with different ranges of pollutant concentrations. There was less evidence available for pollutant concentrations below 5 μg m⁻³ and below 10 μg m⁻³ for PM_{2.5} and NO₂, respectively. The concentration-response functions were not applied below these cut-offs in the main analysis.
- Numbers of baseline asthma admissions for children (0-14 years old) and adults (15-64 years old), and COPD/asthma for the elderly (65+ years old) in each Ward were summed across 2017-2019. These ranged for each Ward from 0 to 64 for asthma admissions in children, less than 10 to 71 for adults and less than 10 to 144 for asthma/COPD admissions in the elderly.

Calculations were then performed in each Ward down to 5 and 10 μ g m⁻³ for PM_{2.5} and NO₂ respectively, before summing the results for each local authority and the whole of London. Calculations were repeated using the same methods and concentration-response functions but using 2016 concentrations (LAEI2016) and 2014-2016 data on asthma admissions.

Results are summarised below. The effects of air pollution on asthma admissions are evident, however there are many other factors driving variations in asthma admissions

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¹ Annual means were used because calculating the health impact for the annual mean is arithmetically equivalent to calculating it for each day and then summing the result, providing there is no threshold. There was a cut-off in this case but all concentrations were above it, so this did not affect the arithmetic equivalence.

other than air pollution. There is also evidence of associations between air pollution and other types of asthma outcomes not covered here, such as asthma symptoms and A&E visits. Further reductions in air pollution in London are likely to benefit asthmatic patients.

Key findings

Exacerbation of asthma by air pollution is estimated to lead to around **700 asthma admissions from 2017 - 2019 in children** in London, 7% of all asthma admissions in children in London. (Asthma admissions may have more than one cause e.g. air pollution may worsen response to an allergen.)

Children are more sensitive than adults, so the numbers for adults are smaller (around 200 adult asthma admissions from 2017-2019).

Chronic obstructive pulmonary disease (COPD), another respiratory disease similar to asthma particularly found in smokers, is more common in the elderly and difficult to distinguish from asthma. Results for the elderly therefore combined asthma and COPD.

Exacerbation of asthma and COPD by air pollution is estimated to lead to around **900** asthma/COPD admissions from **2017-2019** in the elderly in London.

The total across these age groups is over **1,700 air pollution-associated asthma and COPD** admissions, with asthma admissions in children accounting for over a third of these admissions.

The air pollution attributable asthma admissions in children were estimated to have reduced by 30% since 2016 (from approximately 1,000 to 700). The equivalent reductions for asthma in adults and COPD/asthma in the elderly were 27% (from around 250 to 180) and 26% (from around 1,200 to 900), respectively. The percentage reductions were similar or smaller for NO₂ no cut-off and PM_{2.5} with or without the cut-off. These percentage reductions, however, can be attributed to the reductions in air pollution concentrations, as baseline asthma admissions showed similar distribution in the two time periods and the concentration-response functions used were the same.

The above estimates are based on levels of nitrogen dioxide (NO₂) above 10 μg m⁻³. Whether concentrations below 10 μg m⁻³ have effects is much less certain given the more limited data at lower concentrations. Air pollution attributable asthma admissions for 2019 calculated down to zero levels were larger (1,000, 300 and 1,400 for children, adults and the elderly (with COPD)) but more uncertain.

Calculations were also done for PM_{2.5} concentrations above 5 μ g m⁻³. This gave smaller results that probably overlap to some extent with those for NO₂. In fact, as NO₂ is a traffic pollutant, it may represent traffic PM better than PM_{2.5} does (total PM_{2.5} is heavily but not totally influenced by regional sources). As the background evidence for effects of air pollution on asthma is mainly based on NO₂, diesel PM and proximity to traffic, using the results for NO₂ as an indicator for traffic pollution was chosen for the overall summary of the results.

2. Introduction

In 2021, the Greater London Authority (GLA) commissioned researchers from the Environment Research Group (ERG) at Imperial College London to assess the impact on health of the mayoral air quality policies associated with air pollution levels in London (Dajnak et al., 2021). Following this report, the GLA asked the researchers at Imperial to investigate the size of the link between asthma and air pollution in London, using current (2019) and past level (2016) of air pollution. It is accepted that air pollution is linked to exacerbation of asthma² (COMEAP, 1995; WHO, 2013; US EPA 2009, 2013, 2016) with ongoing debate on causation (COMEAP, 2010). This report concentrates on asthma admissions to hospital, particularly in children.

3. Methods

3.1. Air Quality data

The latest London Atmospheric Emissions Inventory (LAEI) versions were used to extract the annual average $PM_{2.5}$ and NO_2 concentration in 2016 (<u>LAEI2016</u>³) and 2019 (<u>LAEI2019</u>⁴). Non-anthropogenic $PM_{2.5}$ was derived by Ward using CMAQ data by subtracting the modelled contribution from natural aerosols sources – here sea-salt - from the total $PM_{2.5}$ modelled as above to generate anthropogenic $PM_{2.5}$ concentrations; consistent with EU guidance (European Commission, 2011).

From 20m grid data to COA concentration

PM_{2.5} and NO₂ annual mean concentrations air pollution data were extracted at 20m grid resolution and intersected with the latest Census Output Areas (COA) from the Office for National Statistics (ONS)⁵ for the Greater London area (a total of 25,053 COAs). Each concentration grid point within each COA was averaged at COA level.

From COA to population-weighted Ward concentration

Population-weighted average concentration (PWAC): Population-weighting was done at Ward level. The COA averaged concentrations were multiplied by the population for each age group separately: children (0-14), adults (15-64) and elderly (65+). The resulting population-concentration product was summed across all COAs in each Ward and then divided by the Ward population for each of the three-age groups separately. The Ward population-weighted means were then used directly in the health impact calculations across all Wards in London (This process allows one health calculation per Ward rather than calculations in each separate COA).

² The clearest evidence is for sulphur dioxide and bronchoconstriction in human volunteer studies – an effect found at much lower concentrations in asthmatics compared with the general population (Johns et al, 2010) but sulphur dioxide concentrations are low.

³https://data.london.gov.uk/dataset/london-atmospheric-emissions-inventory--laei--2016 (Accessed 22 February 2022).

⁴https://data.london.gov.uk/dataset/london-atmospheric-emissions-inventory--laei--2019 (Accessed 22 February 2022).

⁵ https://data.london.gov.uk/dataset/statistical-gis-boundary-files-london (Accessed 22 February 2022).

3.2. Literature search and Meta-analysis

We performed a literature review and meta-analysis following the protocol described in Atkinson et al (2014) and Mills et al (2015). Briefly, we used the database created for the studies above in 2011, concentrating on asthma and omitting mortality terms in the search string (Appendix 1), and a health impact assessment study on the effects of air pollution on asthma in London published in 2019. A search update for studies published up to August 2021 was performed to enhance the databases prepared for the studies mentioned above.

We included studies on the effects of short-term exposure to PM_{2.5} and NO₂ on asthma (ICD-10 code J45) and COPD (ICD-10 code J40-J47) admissions that provided age-specific estimates, i.e. for children, adults or the elderly. Time-series or case-crossover studies were assessed that reported single- or multi-pollutant model estimates. As there are more studies including single-pollutant model results, these were pooled in the knowledge that there was likely to be some overlap between the pollutants. Other study designs and time-series studies with less than 12 months of data (including episode studies) were excluded. We also excluded studies without description of control for season or temperature; studies of emergency room visits that did not separate inpatients from outpatient visits; studies of PM components unclear metrics, such as 'dust storm PM_{2.5}', or sources without PM_{2.5} as a metric; studies using 1-hour maximum instead of 24-hour average NO₂ (the latter is closer to the modelled concentrations), and studies of temperature on mortality that controlled for the effects of pollutants but did not report model estimates.

We also identified a small number of new meta-analyses published after those of Atkinson et al 2014 and Mills et al 2015 (Zheng et al 2015, Lim et al 2016, Orellano et al 2017, Zheng et al 2021). These were not entirely satisfactory for direct use for our burden estimates but were used to identify new studies that were not identified from our search string (see Appendix 1). An electronic reference management system (Endnote X9, Thomson Reuters) was used to build a database and the reported relative risks or odds ratios and other study characteristics, such as the year and season and whether it was a single- or multi-city study, were collected in an Excel spreadsheet (Microsoft Office 2019).

A hierarchical, two-stage approach applying random effects meta-analysis was followed in order to get pooled regional and global health effect estimates. Firstly, a summary estimate from single-city studies within each WHO region was calculated. Then, these estimates were combined with the multi-city study estimates and pooled region-specific estimates and then a global relative risk was calculated. The global estimates were used in the health impact calculations as the number of identified studies was relatively small and we did not want to restrict our database to only those conducted in the UK or in Europe. The "trim and fill" method was used to assess small study bias (Duval and Tweedie 2000).

3.3. Health impact calculations

The study used data held by the UK Small Area Health Statistics Unit (SAHSU), obtained from NHS Digital. We included all emergency hospital admissions derived from Hospital Episode Statistics between 1 January 2014 and 31 December 2019. We included admissions with an asthma diagnosis (defined using the international classification of diseases 10th Revision

(ICD-10) code J45) and chronic obstructive pulmonary disease (COPD) diagnosis (defined as ICD-10 code J40-J47). We stratified admissions by age group to differentiate between children (0-14 years), adults (15-64 years) (asthma admissions only) and older ages (65 years and over) (asthma/COPD combined). Based on the residential postcode at time of admission we aggregated data to Wards. Analysis and presentation of results followed the latest statistical disclosure control guidance from NHS Digital.⁶ For the analysis, the sum of admissions from 2014-2016 and from 2017-2019 were used. This was part of strategies to avoid personal identification of data and also avoided undue influence of unusual years.

<u>Cut-off concentrations</u>

The studies pooled to give the concentration-response function for asthma admissions (the largest grouping) in children were examined for the range of the concentration data in each study. We searched for the minimum concentrations and 5^{th} , 10^{th} and 25^{th} percentiles reported in these studies to investigate the lower part of the distribution of the air pollution data. It was concluded that above the selected cut-offs of $10~\mu g~m^{-3}$ for NO_2 and $5~\mu g~m^{-3}$ for $PM_{2.5}$, the selected concentration-response function was supported by many studies. Below these cut-offs there was only evidence from a smaller set of studies, and even in those studies there would be a much more limited set of datapoints at the concentrations below the cut-offs. Further details are provided in Appendix 1.

Scenario design

The burden of asthma admissions was assessed by calculating the effects of the increment from current levels of air pollution down to zero or the predefined cut-off concentrations at ward level. Although this is representative of the burden of concentrations upwards from (above) zero or the cut-off value, in practical terms it was calculated as the reduction from current levels to zero or the cut-off. This is because the baseline rates of asthma admissions already include the effects of air pollution, and we would not know what baseline rate to use for levels of pollution much lower than those that are present in reality.

For the health impact calculations, we followed the analysis described in Hurley et al (2005). Briefly, we applied the pooled percentage changes in the risk of asthma hospitalization for the corresponding change in air pollution to the baseline number of asthma cases for each age group and pollutant and period of study.

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⁶ <u>Change to Disclosure Control Methodology for Hospital Episode Statistics and Emergency Care Data Set from September 2018</u> The study uses data from the UK Small Area Health Statistics Unit (SAHSU), obtained from NHS Digital. The study was covered by national research ethics approval from the London-South East Research Ethics Committee - reference 17/LO/0846. Data access was covered by the Health Research Authority - Confidentiality Advisory Group under section 251 of the National Health Service Act 2006 and the Health Service (Control of Patient Information) Regulations 2002 - HRA CAG reference: 14/CAG/1039.

4. Results

4.1. Descriptive statistics for the input variables

A summary of the input variables measured at Ward level and used for the burden calculations is provided in Table 1.

Median population-weighted average concentrations for anthropogenic PM $_{2.5}$ were reduced from 12.9 μg m $^{-3}$ in 2016 to 10.4 μg m $^{-3}$ in 2019, while the corresponding values for NO $_2$ were 35.7 μg m $^{-3}$ and 27.8 μg m $^{-3}$, respectively.

For all age groups, the 3-year sum for hospital admissions was similar for the two periods, i.e. with medians of 14 for children, 20 and 21 for adults and 50 and 53 for the elderly.

Table 1 Ward-level descriptive statistics for the population-weighted average concentrations (PWAC) for NO_2 and anthropogenic $PM_{2.5}$ and baseline asthma (asthma and COPD for the elderly) admissions by period of study and age group in London.

Variable	Age	Min	25 th	Mean	Median	75 th	Max
	Group		Percentile	(SD)	(IQR)	Percentile	
	0-14	11.21	12.47	13.03	12.93	13.48	16.16
Anthronogonia				(0.78)	(1.01)		
Anthropogenic PM _{2.5} PWAC 2016	15-64	11.22	12.47	13.04	12.94	13.50	16.26
$(\mu g/m^3)$				(0.8)	(1.03)		
(μg/111°)	65+	11.21	12.47	13.02	12.92	13.48	16.13
				(0.79)	(1.02)		
	0-14	23.97	32.36	36.27	35.73	39.66	52.64
				(5.19)	(7.31)		
NO ₂ PWAC 2016	15-64	24.00	32.38	36.38	35.82	39.87	51.97
(μg/m³)				(5.29)	(7.49)		
	65+	24.09	32.32	36.21	35.70	39.62	51.67
				(5.2)	(7.30)		
	0-14	9.00	10.09	10.57	10.45	10.94	13.66
Anthronogonic				(0.71)	(0.86)		
Anthropogenic PM _{2.5} PWAC 2019	15-64	8.99	10.09	10.58	10.47	10.98	13.76
$(\mu g/m^3)$				(0.72)	(0.89)		
(μg/111)	65+	8.99	10.08	10.56	10.44	10.95	13.58
				(0.71)	(0.87)		
	0-14	18.18	25.21	28.31	27.80	30.92	41.82
				(4.18)	(5.61)		
NO ₂ PWAC 2019	15-64	18.19	25.22	28.39	27.86	30.92	42.02
(μg/m³)				(4.26)	(5.70)		
	65+	18.25	25.19	28.24	27.78	30.79	41.73
				(4.19)	(5.60)		
Hospital	0-14	0	<10 ¹	16	14	21	99
admissions 2014-				(11)	(13)		
2016	15-64	0	12	21	20	28	80
2010				(13)	(16)		

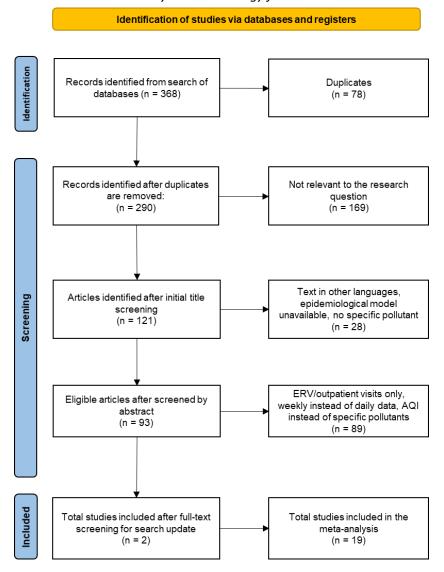
	65+	<10 ¹	36	52	50	65	135
				(23)	(29)		
	0-14	0	<10 ¹	16 (11)	14	21	64
Llocnital					(13)		
Hospital admission 2017-	15-64	<10 ¹	13	22	21	29	71
				(13)	(16)		
2019	65+	<10 ¹	39	56	53	70	144
				(24)	(31)		

¹Exact numbers not reported due to small number suppression

4.2. Literature search and Meta-analysis results

368 studies were picked up by a literature search update that we conducted to inform our previous search (Walton et al 2019). 121 studies were reviewed after removing duplicates and screening by title. Sub-searches by age-group were used to assist the screening process by title and abstract. Studies of emergency room visits were not screened out at this stage as it is often not clear from the abstract whether they separate out inpatient admissions or not. Screening by title and abstract left the full papers for 93 studies to be screened. Screening out studies that only used total emergency room or outpatient visits, without separating out hospital admissions; studies using weekly instead of daily data or those that either did not specify the pollutants under investigation or used Air Quality Indices (AQI) left only 2 studies (Zhang et al 2019, Xie et al 2019). Figure 1 summarizes the above:

Figure 1 Literature search and meta-analysis methodology flow chart.



The 2 studies identified in the update search (and some further studies (Cai et al 2014, Son et al 2013) identified from other sources) were subsequently added to the original database created for our previous health impact assessment study (Walton et al 2019). After checking for overlaps e.g. Xie et al 2019 was from the same city as Zhang et al 2019, we ended up with 19 studies included in the meta-analysis. Some of them reported results for more than one age group, and the final breakdown was 16 studies in children and 9 in adults.

The pooled meta-analytic estimates used in our health impact calculations can be found in Table 2 and Figure 2 (the individual studies included in the meta-analysis can be found in Appendix 2). We estimated a 3.9% (95% confidence interval (CI): 1.5%-6.4%) and 3.2% (1.3%-5.4%) increased risk of asthma hospitalization in children for every 10 μ g m⁻³ increase in NO₂ and PM_{2.5} respectively. No statistically significant association was observed for PM_{2.5} in adults (-0.1% (-2.9%-2.8%)), while for NO₂ the corresponding percentage increase was marginally statistically significant (0.7% (0.0% – 1.5%)). For the elderly, similar forest plots can be found in previous papers (Atkinson et al 2014, Mills et al 2015), as we did not update their estimates.

Figure 2 Summary estimates (95% confidence intervals) for air pollution and asthma hospital admissions by pollutant ($PM_{2.5}$ or NO_2) and age-group. For the elderly, asthma and COPD admissions are combined.

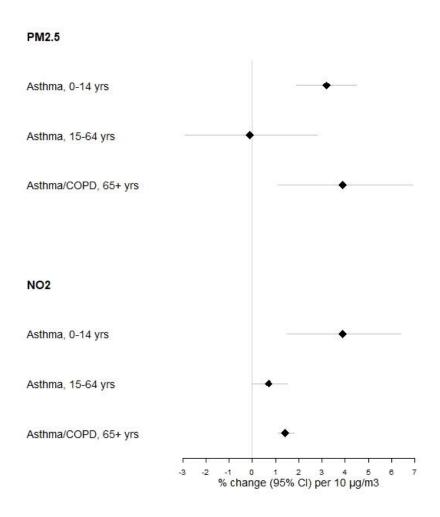


Table 2 Concentration-response functions for air pollution and asthma or asthma/COPD admissions

	% increase	e in hospital admissions per	⁻ 10 μg m ⁻³
Pollutant	Children 0-14	Adults 15-64	Elderly 65+
	Asthma	Asthma	Asthma/COPD
PM _{2.5}	3.2%	-0.1%	3.93%
	(1.9% - 4.5%) ^a	(-2.9% - 2.8%) ^b	(1.06% – 6.89%) ^c
NO ₂	3.9%	0.7%	1.42%
	(1.5% - 6.4%) ^d	(0.0% – 1.5%) ^e	(1.07% - 1.76%) ^f

^aSource: meta-analysis of results from 12 studies, 23 cities for this report (see Appendix 2)

^bSource: meta-analysis of results from 4 studies, 4 cities for this report (see Appendix 2)

^cSource: meta-analysis by Atkinson *et al* 2014, 4 studies, 4 cities (see also Appendix 2)

^dSource: meta-analysis of results from 9 studies, 32 cities for this report (see Appendix 2)

^eSource: meta-analysis of results from 6 studies, 16 cities for this report (see Appendix 2)

^fSource: meta-analysis by Mills *et al* 2015, 7 studies, 7 cities (see Appendix 2)

4.3. Asthma admissions results

We performed the health impact calculations at ward level, but results are reported at both city and local authority level (Table 3 and Figure 3, Appendix 3).

The highest burden estimates for asthma admissions in London amongst the estimates above the cut-off level (10 μ g m⁻³ for NO₂, 5 μ g m⁻³ for PM_{2.5}), were observed for children and NO₂, i.e. 956 (95% CI: 383-1502) admissions in 2014 to 2016 and 666 (95% CI: 265-1057) admissions in 2017 to 2019. The corresponding values for PM_{2.5} are 259 (95% CI: 156-361) and 179 (95% CI: 107-249), respectively.

For combined asthma and COPD admissions in the elderly, the findings were similar for the two pollutants, 1182 (95% CI: 896-1456) for NO_2 and 1028 (95% CI: 285-1757) for $PM_{2.5}$ respectively for the first 3-year period and 873 (95% CI: 661-1077) for NO_2 and 764 (95% CI: 211-1310) for $PM_{2.5}$ for the second.

In general, the asthma admissions attributable to air pollution have reduced substantially (around 20-30%) in the second study period (2017-2019) compared with 2014-2016.

Table 3 2014-2016 and 2017-2019 Asthma admissions estimates (95% confidence intervals) in London from air pollution as indicated by either anthropogenic $PM_{2.5}$ (regional pollution, some local sources) or NO_2 (traffic pollution) – burden from zero levels or lower end of range of concentrations in health studies to current 2016 or 2019 levels of pollution

Scenario ¹	Asthma	Asthma	Asthma/COPD
	admissions	admissions	admissions
	0-14	15-64	65+
Anthropogenic PM _{2.5} (regional pollution	259	_4	1028
/ some local) down to cut-off ³ levels –	(156 - 361)		(285 - 1757)
2014-2016			
NO ₂ (traffic pollution) ² down to cut-off ³	956	249	1182
levels – 2014-2016	(383 - 1502)	(0 - 526)	(896 - 1456)
Anthropogenic PM _{2.5} (regional pollution	407	_4	1611
/ some local) down to zero levels –	(245 - 564)		(449 - 2736)
2014-2016			
NO ₂ (traffic pollution) ² down to zero	1302	342	1629
levels – 2014-2016	(528 - 2024)	(0 - 719)	(1237 - 2003)
Anthropogenic PM _{2.5} (regional pollution	179 [31%] ⁵	_4	764 [26%] ⁵
/ some local) down to cut-off ³ levels –	(107 - 249)		(211 - 1310)
2017-2019			
NO ₂ (traffic pollution) ² down to cut-off ³	666 [30%] ⁵	182 [27%] ⁵	873 [26%] ⁵
levels – 2017-2019	(265 - 1057)	(0 - 385)	(661 - 1077)
Anthropogenic PM _{2.5} (regional pollution	325 [20%] ⁵	_4	1393 [14%] ⁵
/ some local) down to zero levels –	(196 - 452)		(387 - 2372)
2017-2019			
NO ₂ (traffic pollution) ² down to zero	1016 [22%] ⁵	279 [18%] ⁵	1353 [17%] ⁵
levels – 2017-2019	(409 - 1593)	(0 - 588)	(1026 - 1666)

Note: To deal with overlap between pollutants the overall results quoted in the Executive Summary (shown here in bold) were the results with cut-off and the larger of the alternative estimates using $PM_{2.5}$ or NO_2

Results at local authority level are presented below (Figure 3). We present here only the findings for asthma admissions in children, as well as asthma and COPD admissions in the elderly for the two study periods for NO₂ with a cut-off (a full list by local authority including findings in adults can be found in Appendix 3; results are not shown for PM_{2.5} due to a need for large amounts of small number suppression).

Results for local authorities ranged from less than 10 admissions in the City of London, Havering and Kensington and Chelsea to 41 in Waltham Forest for air pollution-associated asthma admissions in children in 2019. The corresponding values for asthma and COPD admissions in the elderly was less than 10 in the City of London to 39 in Southwark in 2019.

In 2016, the highest number of admissions in children and the elderly was 68 in Croydon and 57 in Southwark respectively (the lowest values were observed in the City of London, less than 10).

Note that variations across local authorities are not only influenced by variations in air pollution but also by variations in population size and in other risk factors affecting baseline rates for asthma. For COPD admissions baseline rates are influenced by smoking rates and by trends in smoking rates in the past.

While not shown here, due to small numbers, we also examined the results for air pollution associated asthma admissions by ward. This showed that the wards with the highest and lowest results within each age group and year were consistent across pollutants (despite some variation in concentrations and concentration-response function by pollutant) suggesting spatial variation was driven by spatial variation in the baseline rates of asthma admissions.

The wards with the highest and lowest results were less consistent across age groups and years. This again supports the influence of the baseline rates of asthma admissions, as these will vary across age groups and years, whereas concentrations will not vary across age groups and concentration-response functions will not vary across years.

¹Both PM_{2.5} and NO₂ are 24 hour-averages.

²As the background evidence for effects of air pollution on asthma is mainly based on nitrogen dioxide, diesel PM and proximity to traffic, using the results for NO₂ as an indicator for traffic pollution and with cut-off (more certain than without cut-off) (shown in bold) was chosen for the overall summary of the results.

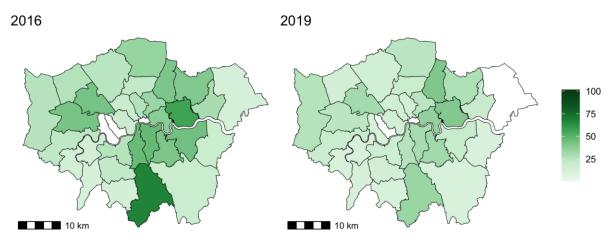
 $^{^3}$ Current concentrations to lowest concentrations covered in several studies (10 μ g m $^{-3}$ for NO₂, 5 μ g m $^{-3}$ for PM_{2.5}). Assumptions for lower cut-offs e.g. the lowest minimum in any study would be between the two results.

⁴The pooled CRF estimated for PM_{2.5} in this age group was not statistically significant, thus due to uncertainty we did not perform health impact calculations

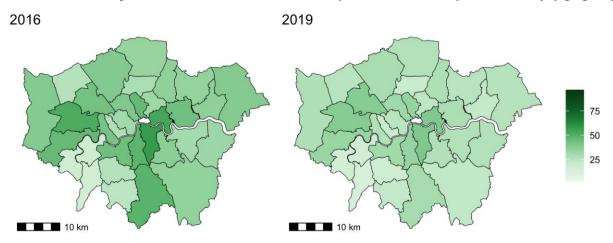
⁵[reduction in the period 2017-2019 compared with 2014-2016]

Figure 3 Spatial distribution of 2014-2016 and 2017-2019 asthma admissions from air pollution as indicated by NO_2 (traffic pollution) across London Boroughs. Estimates are based on NO_2 using cut-off level of 10 μ g/m³ for children and the elderly.

Asthma hospital admissions attributed to NO₂ (above cut-off level) in children (age group 0-14)



Asthma and COPD hospital admissions attributed to NO₂ (above cut-off level) in the elderly (age group 65+)



5. Discussion

These calculations have indicated that air pollution can have a marked impact on asthma admissions in children and adults and on asthma/COPD admissions in the elderly in London. It has also shown that the numbers of air pollution attributable asthma admissions in London have reduced and that this is primarily due to air pollution reductions rather than any changes in the other inputs to the calculations such as baseline hospital admission rates. We published a report in the past on air pollution attributable asthma admissions (Walton et al 2019) but have not highlighted comparisons with this previous report because the methods have changed substantially⁷. Instead, we have re-analysed the data for 2016 using identical methods to that for this update using 2019 pollution data.

The study has a number of strengths:

- Performing updated meta-analyses of previous studies especially for this project.
 The meta-analyses were designed with the use of the summary estimates for
 quantification of asthma admissions in health impact assessments in mind.
 Combining emergency room visits and hospital admissions, as several meta-analyses
 do (Appendix 1) may be appropriate for a general view on whether there is an effect
 of air pollution on asthma exacerbations but is not appropriate for quantification
 because the baseline rates are very different.
- Modelled concentrations at a fine spatial scale (20 x 20m).
- Calculations done at Ward level before summing to local authority and to London.
 This allows the spatial variations in baseline rates for asthma admissions to be taken into account as well as the spatial variations in air pollution.
- Comparing results for 2 different periods (2014-2016 and 2017-2019) using identical methodology.

There are also aspects that could be improved in further work:

- Ozone is not included but there is evidence of associations with asthma admissions (Walton *et al*, 2014).
- As COPD is difficult to distinguish from asthma in the elderly, admissions for these
 causes were combined in the 65+ age group. However, there are also COPD
 admissions at the older end of the 15-64-year age group. These are omitted in this
 analysis.
- The meta-analyses used studies in whatever regions of the world were available.
 This had the advantage of increasing the strength of the evidence in terms of the number of studies but the disadvantage of including studies from locations with higher concentrations and a different composition from the air pollution mixture found in London.
- The meta-analyses were based on single-pollutant model results. Multi-pollutant model results which aim to identify the independent effects of the pollutants were not reviewed but are likely to be too small in number for meta-analysis.

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⁷ One significant reason for the difference between the estimates here and those in the previous report is the use of epiorder 1 in the extract of hospital admissions data for this report which does not count episodes with multiple respiratory consultants involved more than once.

 Additional sensitivity analyses could be done on varying assumptions for the concentration-response functions or the lowest concentrations that are regarded as providing evidence for associations in the epidemiological studies (cut-offs).

The burden for asthma admissions in children in London is larger for children than adults and for NO_2 than $PM_{2.5}$ (Table 3). The latter point was expected because the concentration-response function was larger for NO_2 than for $PM_{2.5}$ and the concentration increment for NO_2 is larger. Adding the results for the two pollutants is not recommended as there is likely to be overlap between the results.

We dealt with the overlap between pollutants by basing the summary of results on studies using NO_2 , arguing that this represented not only NO_2 itself but also traffic PM, the part of PM with the greatest evidence for links with asthma exacerbations. The background evidence for effects of air pollution on asthma is mainly based on nitrogen dioxide (Brown 2015), Diesel/traffic PM (COMEAP, 2010) and proximity to traffic (COMEAP, 2010).

PM can also contain pollen fragments, lipopolysaccharides (derived from bacterial cell walls) (at very low levels in $PM_{2.5}$) and fungal spores (Robinson et al, 2013), all of which can act as allergens/triggers of inflammation. These are found to a greater extent in the coarse fraction but if small fragments are in the $PM_{2.5}$ fraction, then they would not be expected to be particularly highly correlated with NO_2 . This might argue for some of the $PM_{2.5}$ associations being independent of traffic pollution.

It is not known whether the increased number of asthma admissions on higher air pollution days would not have happened at all if pollution levels had been lower or whether the air pollution accelerated an already existing decline in disease status in asthmatic patients that would have resulted in a hospital admission at a later date. It is still likely that reductions in air pollution would reduce numbers of hospital admissions but there is some uncertainty as to what degree assuming the hospital admissions are additional results in an overestimate of the reductions.

It is important to put these figures in context. For example, the total number of asthma admissions in children over 2017-2019 is 10,000, compared with around 700 estimated to be linked to air pollution here, about 7%. The proportion is smaller for adults (around 1%). There are other important triggers for asthma exacerbations such as respiratory infections and allergens. The studies on NO₂ and airway hypersensitivity show that prior exposure to NO₂ increases the response of the airways to later exposure to histamine, a chemical involved in the allergenic response (Brown 2015). So, it is entirely possible for more than one trigger to contribute to an admission to hospital for asthma.

Further work is needed both in terms of expanding the range of original research studies and in developing health impact assessment of the effects of air pollution in London.

- If more time-series studies were available to derive the concentration response functions it might be possible to base a concentration-response function on studies in Europe.
- While the results in this report focus on admissions to hospital for asthma, these are not the only way of representing the effect of air pollution on asthma and do not

represent the whole picture. They are one of the more reliable indicators, both from the point of view of the original research studies and due to the availability of routine statistics on hospital admissions. Some initial investigation of the potential for quantification of wider asthma outcomes was described in Appendix 6 of our previous report (Walton et al 2019). Some of these points and an update of some of the evidence is provided in the bullet points below.

- There are substantial numbers of studies on emergency room visits for asthma in the
 US (US EPA, 2021,2019,2013,2016; Zheng et al, 2021) but this does not have an exact
 health care system equivalent in the UK (covers a range between an A&E visit and a
 GP consultation). There is one study in London of A&E visits (Atkinson et al 1999)
 although using results of a single study is less robust.
- There are WHO recommendations for quantification of asthma symptoms (WHO, 2013) that are probably worth quantifying, although baseline rates from research studies in other locations, rather than routine statistics for London, would have to be used.
- There is also debate about air pollution as a cause of asthma (COMEAP, 2010). There is an association with asthma incidence (Gehring et al 2015; Liu et al 2021) but not prevalence (Molter et al 2015; Fuertes et al 2020) from large studies including several cohorts across Europe. This may suggest that air pollution may be affecting a subset of asthma that is more reversible than the classic allergic asthma that starts in childhood and lasts a lifetime. If it is more reversible, then it may be that quantifying symptoms, hospital admissions and all-cause mortality (for the rare cases of asthma deaths) would an appropriate way to quantify air pollution effects on asthma. This needs further research and discussion, particular in the context of growing evidence on different sub-types of asthma. In addition to the possibility that many in the population may have a more reversible type of asthma, there is also the possibility that those with other sub-types of asthma may be particularly susceptible, even if the overall number of these sub-types is small in public health terms.

In conclusion, air pollution effects on asthma admissions in London remain although the concentration reductions between 2016 and 2019 have meant that the number of air pollution-attributable asthma admissions has declined.

6. Appendices

6.1. Appendix 1: Literature search methods

Selecting concentration-response functions

The starting point was a Department of Health commissioned project reviewing studies up to May 2011 published as Atkinson et al 2014 and Mills et al 2015 for $PM_{2.5}$ and NO_2 . An update was performed in 2018 to identify further studies published after 2011 that can be found in Walton et al 2019. Finally, we performed another search update in August 2021 and build our final database with studies examining the association between air pollution and asthma hospital admissions.

Search string

The search of literature databases used the same search string as in the projects above although it omitted terms relating to mortality and to cardiovascular disease to concentrate on asthma.

Reviews were checked for additional studies.

The studies were sifted for quality using the same protocol as Atkinson et al 2014 and Mills et al 2015. This included omitting time-series studies with less than 12 months of data and ensuring studies had appropriate control for temperature and season.

Inclusion criteria: Time-series studies or case-crossover studies, asthma admissions, children, adults or elderly separately with quantitative information on single-pollutant model relative risks or odds ratios for NO₂ or PM_{2.5}.

Exclusion criteria: Other study designs, time-series studies with less than 12 months of data (including episode studies), studies without description of control for season or temperature, studies of emergency room visits that did not separate inpatients from outpatient visits, pollutant metrics that were unclear e.g. 'dust storm PM_{2.5}', studies of PM components or sources without PM_{2.5} as a metric, studies of temperature on mortality that controlled for the effects of pollutants.

368 studies were picked up by the latest literature search update, 121 studies after removing duplicates and screening by title. Sub-searches by age-group were used to assist the screening process by title and abstract and 93 papers were fully reviewed. Studies of

emergency room visits were not screened out at this stage as it is often not clear from the abstract whether they separate out inpatient admissions or not. Screening out studies that only used total emergency room visits, without separating out hospital admissions, left just 1 study. This was subsequently supplemented by 18 studies identified in our second stage search update for our previous report (Walton et al 2019). A final set of 19 studies was included in the meta-analysis, 16 in children and 9 in adults (some studies provided estimates for more than one age group).

A sub-search on reviews identified 5 reviews. Of the 5 reviews identified, 1 was a qualitative narrative review (Delzell 2013). The other 4 were:

Zheng et al (2015) Emergency room visits and hospital admissions combined, all ages. Subgroup analysis indicated larger estimates for children and the elderly, but these were still for emergency room visits and hospital admissions combined. Stratification of the all-ages result into hospital admissions and emergency room visits was reported to result in larger estimates for hospital admissions but no quantitative information was given in the main paper and there was no additional separation by age group.

Lim et al (2016) Mainly emergency room visits and hospital admissions combined, children only, PM_{2.5} only. A separate summary estimate for hospital admissions was given, although which studies were included was not specified. These were inferred by screening the total list of studies in the combined emergency room visits and hospital admission analysis. This indicated that the summary allowed more than one study per city (it could be argued that these are not independent of each other – a requirement for the meta-analytical approach). It also included more than one estimate per study (for different age groups for example). It did not include 6 studies that were included in Atkinson et al (2014). It was therefore unclear that it provided an update to the earlier study rather than just a different approach. It was therefore decided not to use the summary estimate in Lim et al direct but to add any new studies identified in this analysis not picked up in the literature search in a new meta-analysis.

Orellano et al (2017) Combined emergency room visits and hospital admissions in their summary estimates. Separate summary estimates were provided for children and adults, but emergency room visits and hospital admissions were not separated. This review was screened for additional studies, some of which did in fact separate out hospital admissions.

Zheng et al (2021) Combined emergency room visits and hospital admissions in their summary estimates. Separate summary estimates were provided by age group and type of admission but not simultaneously.

For combined asthma/COPD admissions in the elderly, our sub-search in Walton et al 2019 identified 12 studies. Further screening did not identify any new studies and no sub-search was conducted in 2021. A review by Moore et al (2016) was identified but it covered COPD admissions alone not combined with asthma. So, the summary estimates from Atkinson et al 2014 ($PM_{2.5}$) and Mills et al 2015 (NO_2) were used.

For asthma admissions in adults and children for NO₂ and PM_{2.5} new meta-analyses were performed.

The updated meta-analyses used the same protocol as Atkinson et al (2014) and Mills et al (2015) e.g. 1 estimate per study location (priority was given to a city analysis within a multicity study, otherwise the most recent study was used unless there were specific reasons against). A hierarchical approach was used for single and multi-city estimates as explained in Appendix 2.

Odds ratios were converted to relative risks using prevalence data for asthma admissions if possible, if not general asthma prevalence in the relevant city⁸ was checked to assess whether prevalence of asthma hospital admissions was likely to be sufficiently low for the odds ratio to be similar to the relative risk. This was indeed the case.

There is a debate regarding whether it is best to use local or regional studies that have a more relevant pollutant mixture and population characteristics or wider global groups of studies. There is quite a bit of variation across studies just by chance (repeated studies within the same city can vary substantially too) so generally it is better to use a larger number of studies. Usually there are not sufficient numbers of studies from one country (the aim is to have at least 4 studies for meta-analysis). Ideally, we would use studies from Europe but, in practice, the number of studies in Europe was small and we chose to use all studies from across the world.

Application of the above protocols reduced the number of studies providing estimates further. The final set of studies contributing estimates is given in Appendix 2.

Selection of Cut-offs

The original studies pooled to give the concentration-response function for asthma admissions (the largest grouping) in children were examined for the range of the concentration data in each study. Various groups have approached this in different ways. The approach followed by the Global Burden of Disease project for PM_{2.5} was to use a counterfactual bounded by the minimum value and 5th percentile of the concentrations in the largest cohort study used to derive the coefficient (Burnett et al., 2014, Lim et al., 2012). COMEAP (2018) in its report on nitrogen dioxide, examined minimums, 5th and 10th percentiles in the range of studies used in the meta-analysis of long-term exposure to nitrogen dioxide and mortality. We took a similar approach.

We looked at the studies included in our meta-analyses (Appendix 2) for the descriptive statistics of the air pollution data that were used in their epidemiological models. In particular, we searched for minimum concentrations and 5th, 10th and 25th percentiles to get an idea of the lower part of the distribution of the air pollution exposure data. However, most studies did not report all the statistics mentioned above, but rather mainly the

 $^{^{\}rm 8}$ Thanks to Li Yan King's College, London for checking as thma prevalence in Chongqing.

minimum and 25th percentiles were reported. Thus, we examined the range of these statistics in order to select appropriate cut-off values for the two pollutants.

For NO₂, we identified a range in the minimum values from approximately 4.5 to 36 μg m⁻³. The upper limit of this range though was an outlier, while most of the minimum values were between 4.5 and 13.3 μg m⁻³. Moreover, the 25th percentile of the reported concentrations ranged from 15 to 55 μg m⁻³. Therefore, we chose a cut-off value of 10 μg m⁻³ as representative of the lower end of the range of NO₂ daily concentrations.

For PM_{2.5}, minimum values ranged from 0.25 to 18 μg m⁻³, but 18 was an outlier as the majority of values were between 0.25 and 2.3 μg m⁻³. Similarly, 25th percentiles ranged from 4.5 to 35.4 μg m⁻³, but most studies reported numbers below 8 μg m⁻³. Thus, we regarded that a value between 3 and 8 μg m⁻³ for the lower end of the range of PM_{2.5} concentrations was relatively plausible. For a single figure in the middle of this range we chose 5 μg m⁻³.

These calculations and assumptions were based on the epidemiological asthma studies in children used for the quantification of the concentration-response functions. We, also, checked the summary measures of the exposure data in the studies in other age groups included in our meta-analyses and their reported statistics were on average within the same ranges.

It was concluded that above the selected cut-offs of 10 μ g m⁻³ for NO₂ and 5 μ g m⁻³ for PM_{2.5}, the selected concentration-response function was supported by many studies. Below these cut-offs there was only evidence from a smaller set of studies, and even in those studies there would be a much more limited set of datapoints at the concentrations below the cut-offs.

6.2. Appendix 2: Meta-Analyses

A hierarchical, two-stage approach was followed (Atkinson *et* al 2014) in order to get a pooled estimate for the relative risk. Firstly, a summary estimate from single-city studies within each WHO region was calculated. Then, these estimates were combined with the multi-city study estimates and pooled region-specific estimates and then a global relative risk were calculated.

PM_{2.5} and Asthma Hospital Admissions – Children

In total, 12 studies were included in the meta-analysis from 4 different WHO regions, i.e. 5 from the Americas (AMR A), 2 from Europe (EUR A) and 5 from Western Pacific (1 WPR A and 4 WPR B). The studies are:

City, Author, Year	WHO Region	Single- or Multi-City Study	RR (per 10 μg m ⁻³)	95% CI
Anchorage, Chimonas, 2007	AMR A	Single	0.876	(0.637, 1.206)
Toronto, Lin, 2002	AMR A	Single	0.936	(0.872, 1.004)
New York, Goodman, 2017	AMR A	Single	1.022	(1.001, 1.043)
St Louis, Winquist, 2012	AMR A	Single	1.056	(0.984, 1.133)
California, Ostro, 2009	AMR A	Multi	1.023	(0.994, 1.054)
West Midlands, Anderson, 2001	EUR A	Single	1.033	(0.995, 1.074)
Copenhagen, Iskandar, 2012	EUR A	Single	1.192	(1.084, 1.285)
Australia & New Zealand, Barnett, 2005	WPR A	Multi	1.027	(0.936, 1.126)
Shanghai, Hua, 2014	WPR B	Single	1.043	(1.034, 1.052)
Chongqing, Ding, 2017	WPR B	Single	1.021	(0.992, 1.051)
Hong Kong, Ko, 2007	WPR B	Single	1.024	(1.013, 1.035)
Hefei, Zhang, 2019	WPR B	Single	1.063	(1.029, 1.097)

First stage: Pooling single-city study estimates

WHO Region	Single-city study Pooled RR	95% CI
AMR A	1.003	(0.950, 1.059)
EUR A	1.104	(0.960, 1.269)
WPR A	No study	-
WPR B	1.036	(1.021, 1.051)

Weights:

AMR A: Chimonas=2.71%, Lin= 26.24%, Goodman= 44.67%, Winquist= 26.38%.

Heterogeneity: I²=59.7%

EUR A: Anderson=53.7%, Iskandar=46.3%. Heterogeneity: I²=88.9%

WPR B: Hua=36.22%, Ding=15.97%, Ko=33.69%, Zhang=14.11%. Heterogeneity:

 $I^2=70.9\%$

Second stage: Pooling multi-city study and previous estimates

WHO Region	Multi-city study Pooled RR	95% CI
AMR A	1.019	(0.993, 1.045)
EUR A	1.104	(0.960, 1.269)
WPR A	1.027	(0 .936, 1.126)
WPR B	1.036	(1.021, 1.051)

Weights:

AMR A: Single-city studies=22.84%, Ostro=77.16% Heterogeneity: I²=0%

EUR A: Single-city studies=100%

WPR A: Barnett=100%

WPR B: Single-city studies=100%

Global summary estimate

WHO Region	Pooled RR	95% CI
Global	1.032	(1.019, 1.045)

Weights:

AMR A=23.98%, EUR A=0.82%, WPR A=1.86%, WPR B=73.34%

Heterogeneity:

 $I^2 = 0\%$

TRIM 'N' FILL
First stage: Pooling single-city study estimates

WHO Region	Single-city study Pooled RR	95% CI
AMR A	1.003	(0.950, 1.059)
EUR A	1.034	(0.908, 1.177)
WPR A	No study	-
WPR B	1.036	(1.021, 1.051)

Weights:

AMR A: Chimonas=2.71%, Lin= 26.24%, Goodman= 44.67%, Winquist= 26.38%. **Heterogeneity**: I²=59.7% **NO TRIMMING PERFORMED**

EUR A: Anderson=35.98%, Iskandar=32.01%, **1 Filled study**=32.01% **Heterogeneity**: I^2 =90.8%

WPR B: Hua=36.22%, Ding=15.97%, Ko=33.69%, Zhang=14.11%. Heterogeneity: I^2 =70.9% NO TRIMMING PERFORMED

Second stage: Pooling multi-city study and previous estimates

WHO Region	Multi-city study Pooled RR	95% CI
AMR A	1.019	(0.993, 1.045)
EUR A	1.034	(0.908, 1.177)
WPR A	1.027	(0 .936, 1.126)
WPR B	1.036	(1.021, 1.051)

Weights:

AMR A: Single-city studies=22.84%, Ostro=77.16% **Heterogeneity**: I²=0% **NO TRIMMING PERFORMED**

EUR A: Single-city studies=100% NO TRIMMING PERFORMED

WPR A: Barnett=100% NO TRIMMING PERFORMED

WPR B: Single-city studies=100% NO TRIMMING PERFORMED

Global summary estimate

WHO Region	Pooled RR	95% CI
Global	1.031	(1.018, 1.045)

Weights:

AMR A=23.95%, EUR A=0.95%, WPR A=1.85%, WPR B=73.25%

Heterogeneity:

 $I^2 = 0\%$

PM_{2.5} and Asthma Hospital Admissions – Adults

We have only 4 studies in total:

City, Author, Year	WHO Region	Single- or Multi-City Study	RR (per 10 μg m ⁻³)	95% CI
New York, Goodman, 2017	AMR A	Single	0.995	(0.981, 1.010)
St Louis, Winquist, 2012	AMR A	Single	1.031	(0.972, 1.094)
West Midlands, Anderson, 2001	EUR A	Single	0.952	(0.904, 1.001)
Hong Kong, Ko, 2007	WPR B	Single	1.018	(1.008, 1.028)

The same hierarchical, two-stage approach as in the previous meta-analysis was followed, but in this case we had only single-city studies and only two were from the same WHO region. We have:

First stage: Pooling single-city study estimates

WHO Region	Single-city study Pooled RR	95% CI
AMR A	1.001	(0.976, 1.027)
EUR A	0.952	(0.904, 1.001)
WPR A	No study	-
WPR B	1.018	(1.008, 1.028)

Weights:

AMR A: Goodman= 83.59%, Winquist= 16.41%. Heterogeneity: I²=23.7%

EUR A: Anderson=100%

WPR B: Ko=100%

Second stage: Pooling multi-city study and previous estimates – Omitted, NO multi-city studies

Global summary estimate

WHO Region	Pooled RR	95% CI
Global	0.999	(0.971, 1.028)

Weights:

AMR A=34.86%, EUR A=19.14%, WPR B=46.00%

Heterogeneity:

 $I^2=73.4\%$

TRIM 'N' FILL
First stage: Pooling single-city study estimates

WHO Region	Single-city study Pooled RR	95% CI
AMR A	0.995	(0.969, 1.021)
EUR A	0.952	(0.904, 1.001)
WPR A	No study	-
WPR B	1.018	(1.008, 1.028)

Weights:

AMR A: Goodman= 68.55%, Winquist= 15.72%, **1 Filled study**=15.72%.

Heterogeneity: I²=28.3%

EUR A: Anderson=100%, NO TRIMMING PERFORMED

WPR B: Ko=100% Heterogeneity: I²=100% NO TRIMMING PERFORMED

Second stage: Pooling multi-city study and previous estimates – Omitted, NO multi-city studies

Global summary estimate

WHO Region	Pooled RR	95% CI
Global	0.996	(0.966, 1.027)

Weights:

AMR A=35.08%, EUR A= 20.32%, WPR B= 44.61%

Heterogeneity: 1^2 =76.6%.

PM_{2.5} and COPD/Asthma Hospital Admissions – Elderly

Used estimate from Atkinson et al 2014 given in the supplementary material. The estimate labelled COPD excluding asthma is in fact the one for COPD including asthma (the original studies were checked). This included the following:

City, Author, Year	WHO Region	Single- or Multi-City Study	RR (per 10 μg m ⁻³)	95% CI
Andersen 2008	EUR A	Single, Copenhagen	1.000	(0.9025, 1.108)
Halonen, 2009	EUR A	Single, Helsinki	1.0417	(1.0125, 1.0709)
Moolgavkar, 2000	AMR A	Single, Los Angeles County	1.02	(1.0037, 1.0363)
Ito, 2003 in Health Effects Institute, 2003 (Update of Lippmann et al 2000)	AMR A	Single, Wayne County (Detroit)	1.0117	(0.9714,1.052)

Pooled overall summary estimate 1.0236 (1.01, 1.0373)), I^2 : 32% (EUR A 1.0393 (1.0106, 1.0689) only 2 studies; AMR A 1.019 (1.0037, 1.0346) only 2 studies). The corresponding forest plot can be found in the supplementary material of Atkinson et al 2014.

NO₂ and Asthma Hospital Admissions in Children

In total, 9 studies were included in the meta-analysis from 3 WHO regions, i.e. 3 from Europe (EUR A), 2 from WPR A and 4 from WPR B. The studies are:

City, Author, Year	WHO Region	Single- or Multi-City Study	RR (per 10 μg m ⁻³)	95% CI
4 European Cities, Sunyer, 1997	EUR A	Multi	1.005	(1.001, 1.009)
EpiAir Italy, Colais, 2009	EUR A	Multi	1.013	(0.989, 1.038)
Copenhagen, Iskandar, 2012	EUR A	Single	1.078	(1.032, 1.125)
Fukuoka, Ueda, 2010	WPR A	Single	1.057	(1.011, 1.105)
Australia & New Zealand, Barnett, 2005	WPR A	Multi	1.062	(1.002, 1.125)
Hefei, Zhang 2019	WPR B	Single	1.260	(1.151,1.379)
Chongqing, Ding, 2017	WPR B	Single	1.168	(1.011, 1.350)
Hong Kong, Ko, 2007	WPR B	Single	1.039	(1.028, 1.050)
8 Korean cities, Son 2013	WPR B	Multi	1.017	(1.000, 1.035)

First stage: Pooling single-city study estimates

WHO Region	Single-city study Pooled RR	95% CI
AMR A	No study	-
EUR A	1.078	(1.033, 1.126)
WPR A	1.057	(1.011, 1.105)
WPR B	1.145	(0.993, 1.321)

Weights:

EUR A: Iskandar=100% WPR A: Fukuoka=100%

WPR B: Zhang=33.56%, Ko=38.69%, Ding=27.74%. **Heterogeneity**: I²=89.8%

Second stage: Pooling multi-city study and previous estimates

WHO Region	Multi-city study Pooled RR	95% CI
AMR A	No Study	-
EUR A	1.024	(0.994, 1.055)
WPR A	1.059	(1.022, 1.096)
WPR B	1.056	(0.948, 1.176)

Weights:

EUR A: Single-city studies=22.63%, Sunyer=43.67%, Colais=33.70%. **Heterogeneity**: I^2 =80.8%

WPR A: Fukuoka=63.09%, Single-city studies=36.91%. **Heterogeneity**: I²=0.0% WPR B: Single-city studies=31.35%, Son=68.65%. **Heterogeneity**: I²=61.6%

Global summary estimate

WHO Region	Pooled RR	95% CI
Global	1.039	(1.015, 1.064)

Weights:

EUR A=55.02%, WPR A=40.35%, WPR B=4.63%

Heterogeneity:

 $1^2=5.9\%$

TRIM 'N' FILL First stage: Pooling single-city study estimates

WHO Region	Single-city study Pooled RR	95% CI
AMR A	No study	-
EUR A	1.078	(1.033, 1.126)
WPR A	1.057	(1.011, 1.105)
WPR B	1.145	(0.993, 1.320)

Weights:

EUR A: Iskandar=100% NO TRIMMING PERFORMED

WPR A: Ueda=100% **NO TRIMMING PERFORMED**

WPR B: Zhang=33.56%, Ko=38.69%, Ding=27.74%. **Heterogeneity**: I²=89.8% **NO**

TRIMMING PERFORMED

Second stage: Pooling multi-city study and previous estimates

WHO Region	Multi-city study Pooled RR	95% CI
AMR A	No Study	-
EUR A	1.024	(0.994, 1.055)
WPR A	1.057	(1.026, 1.089)
WPR B	1.056	(0.948, 1.176)

Weights:

EUR A: Single-city studies=22.63%, Sunyer=43.67%, Colais=33.70%. **Heterogeneity**: I^2 =80.8% **NO TRIMMING PERFORMED**

WPR A: Single-city studies=46.08%, Barnett=26.96%, **1 Filled study**=26.96%. **Heterogeneity**: I^2 =0%

WPR B: Single-city studies=31.35%, Son=68.65%. Heterogeneity: I^2 =61.6% NO TRIMMING PERFORMED

Global summary estimate

WHO Region	Pooled RR	95% CI
Global	1.041	(1.017, 1.065)

Weights:

EUR A=48.38%, WPR A=47.19%, WPR B=4.44%

Heterogeneity:

 $I^2=11.8\%$

NO₂ and Asthma Hospital Admissions in Adults

In total, 6 studies were included in the meta-analysis from 3 WHO regions. Two studies were from Europe (EUR A), 1 from WPR A and 3 from WPR B. The studies are:

City, Author, Year	WHO Region	Single- or Multi-City Study	RR (per 10 μg m ⁻³)	95% CI
4 European Cities, Sunyer, 1997	EUR A	Multi	1.006	(1.001, 1.011)
Rome, Michelozzi, 2000	EUR A	Single	1.024	(0.991, 1.058)
Hong Kong, Ko, 2007	WPR B	Single	1.018	(1.007, 1.029)
Sydney, Morgan 1998	WPR A	Single	1.013	(0.982, 1.045)
Shanghai, Cai 2014	WPR B	Single	1.026	(1.012, 1.041)
8 Korean cities, Son 2013	WPR B	Multi	0.989	(0.969, 1.010)

First stage: Pooling single-city study estimates

WHO Region	Single-city study Pooled RR	95% CI
AMR A	No study	-
EUR A	1.024	(0.991, 1.058)
WPR A	1.013	(0.982, 1.045)
WPR B	1.021	(1.012, 1.030)

Weights:

EUR A: Michelozzi=100% WPR A: Morgan=100%

WPR B: Ko=63.74%, Cai=36.26%. **Heterogeneity**: I²=0.0%

Second stage: Pooling multi-city study and previous estimates

WHO Region	Multi-city study Pooled RR	95% CI
AMR A	No Study	-
EUR A	1.007	(0.999, 1.015)
WPR A	1.013	(0.982, 1.045)
WPR B	1.007	(0.976, 1.038)

Weights:

EUR A: Single-city studies=5.85%, Sunyer=94.15%. Heterogeneity: I²=7.3%

WPR A: Single-city studies=100%

WPR B: Single-city studies=54.67%, Son=45.33%. Heterogeneity: I²=86.7%

Global summary estimate

WHO Region	Pooled RR	95% CI
Global	1.007	(1.000, 1.015)

Weights:

EUR A=88.01%, WPR A=5.93%, WPR B=6.06%

Heterogeneity:

 $I^2=0\%$

TRIM 'N' FILL First stage: Pooling single-city study estimates

WHO Region	Single-city study Pooled RR	95% CI
AMR A	No Study	-
EUR A	1.024	(0.991, 1.058)
WPR A	1.013	(0.982, 1.045)
WPR B	1.018	(1.010, 1.026)

Weights:

EUR A: Michelozzi=100% NO TRIMMING PERFORMED

WPR A: Morgan=100% NO TRIMMING PERFORMED

WPR B: Ko=44.3%, Cai=27.85%, **1 Filled study**=27.85%. **Heterogeneity**: I²=16.2%

Second stage: Pooling multi-city study and previous estimates

WHO Region	Multi-city study Pooled RR	95% CI		
AMR A	No Study	-		
EUR A	1.006	(0.997, 1.014)		
WPR A	1.013	(0.982, 1.045)		
WPR B	1.005	(0.978, 1.034)		

Weights:

EUR A: Single-city studies=6.5%, Sunyer=87.0%, **1 Filled study**=6.5%. **Heterogeneity**: I^2 =9.5%

WPR A: Single-city studies=100% NO TRIMMING PERFORMED

WPR B: Single-city studies=55.79%, Son=44.21%. **Heterogeneity**: I²=84.1% **NO TRIMMING PERFORMED**

Global summary estimate

WHO Region	Pooled RR	95% CI
Global	1.006	(0.998, 1.014)

Weights:

EUR A=85.4%, WPR A=6.5%, WPR B=8.1%

Heterogeneity:

I²=0%

NO₂ and COPD/Asthma Hospital Admissions – Elderly

Used estimate from Mills et al 2015 given in the supplementary material. This included the following:

City, Author, Year	WHO Region	Single- or Multi-City Study	RR (per 10 μg m ⁻³)	95% CI
Andersen 2008	EUR A	Single,	1.0508	(1.0087,
7.11.001.5011.2000	201171	Copenhagen	1.0300	1.0929)
Halonen, 2009	EUR A	Single, Helsinki	1.0237	(1.0025,
11011011011, 2003	LONA	Siligic, Helsiliki	1.0237	1.045)
Moolgavkar, 2000	AMR A	Single, Cook	1.0105	(1.0036,
iviooigavkai, 2000	AIVIN A	County	1.0103	1.0173)
	00 AMR A	Single, Los		/1 0007
Moolgavkar, 2000		Angeles	1.0131	(1.0097,
		County		1.0164)
Moolgovkor 2000	AMR A	Single,	1 022	(1.0057,
Moolgavkar, 2000	AIVIK A	Maricopa	1.023	1.0403)
		Single, Wayne		
Lippmann, 2000	AMR A	County	1.0117	(0.9714,1.052)
		(Detroit)		
Health Effects	W/DD D	Single, Hong	1 0151	(1.0108,
Institute, 2010	WPR B	Kong	1.0151	1.0193

Pooled overall summary estimate 1.0142 (1.0107, 1.0176)) I^2 30.8% (EUR A 1.0314 (1.0076, 1.0558) only 2 studies; AMR A 1.0128 (1.0099, 1.0158) (only 2 studies, but 4 areas). The corresponding forest plot can be found in the supplementary material of Mills et al 2015.

Forest Plots for Meta-Analysis

Figure S1 Forest plot with study characteristics and individual and pooled epidemiological estimates for the $PM_{2.5}$ effects on asthma hospital admissions in children (0-14 years old).

WHO Region/ Country	City	Author	Year	Lag	Study period		RR (95% CI) per 10 μg/m3 PM2.5
AMR A- Multi city USA	6 California Counties	Ostro	2009	lag 3	2000-2003	-	1.023 (0.994, 1.054)
AMR A-Single city							
Alaska	Anchorage	Chimonas	2007	lag 0	1999-2003	€ ♦	0.876 (0.637, 1.206)
Canada	Toronto	Lin	2002	lag 6	1980-1994	•	0.936 (0.872, 1.004)
USA	New York	Goodman	2017	lag 0	1999-2009	-	1.022 (1.001, 1.043)
USA	St Louis	Winquist	2012	lag 0-4	2001-2007		1.056 (0.984, 1.133)
EUR A- Single city							
Denmark	Copenhagen	Iskandar	2012	lag 0-4	2001-2008		1.192 (1.084, 1.285)
UK	West Midlands	Anderson	2001	lag 0-1	1994-1996	•	1.033 (0.995, 1.074)
WPR A-Multi city Australia & New Zealand	Australia 5 cities New Zealand 2 cities	Barnett	2005	lag 0-1	1998-2001	•	1.027 (0.936, 1.126)
WPR B-Single city							
China	Chongqing	Ding	2017	Best lag	2013	0	1.021 (0.992, 1.051)
China	Hefei	Zhang	2019	lag 0-1	2015-2016		1.063 (1.029, 1.097)
China	Hong Kong	Ko	2007	lag 0-5	2000-2005	-	1.024 (1.013, 1.035)
China	Shanghai	Hua	2014	lag 0-5	2007-2012		1.043 (1.034, 1.052)
Pooled Estimate						0.9 0.95 1 1.05 1.1	1.032(1.019, 1.045)

Figure S2 Forest plot with study characteristics and individual and pooled epidemiological estimates for the $PM_{2.5}$ effects on asthma hospital admissions in adults (15-64 years old).

WHO Region/ Country	City	Author	Year	Lag	Study period		RR (95% CI) per 10 µg/m3 PM2.5
AMR A-Single city							
USA	New York	Goodman	2017	lag 0	1999-2009	-	0.995 (0.981, 1.010)
USA	St Louis	Winquist	2012	lag 0-4	2001-2007	•	1.031 (0.972, 1.094)
EUR A-Single city							
UK	West Midlands	Anderson	2001	lag 0-1	1994-1996	•	0.952 (0.904, 1.001)
WPR B-Single city							
China	Hong Kong	Ко	2007	lag 0-5	2000-2005	+	1.018 (1.008, 1.028)
Pooled Estimate						•	0.999 (0.971, 1.028)
						0.9 0.95 1 1.05 1.1	

Figure S3 Forest plot with study characteristics and individual and pooled epidemiological estimates for the NO_2 effects on asthma hospital admissions in children (0-14 years old).

WHO Region/ Country	City	Author	Year	Lag	Study period		RR (95% CI) per 10 µg/m3 NO2
EUR A-Multi city Europe Italy	3 European cities 9 Italian cities	Sunyer Colais	1997 2009	lag 0 up to 3 lag 0	1986-1992 2001-2005	•	1.005 (1.001, 1.009) 1.013 (0.989, 1.038)
EUR A-Single city Denmark	Copenhagen	Iskandar	2012	lag 0-4	2001-2008		1.078 (1.033, 1.126)
WPR A-Multi city Australia & New Zealand	Australia 5 cities New Zealand 2 cities	Barnett	2005	lag 0-1	1998-2001	•	1.062 (1.002, 1.125)
WPR A- Single city Japan	Fukuoka	Ueda	2010	lag 2-3	2001-2007		1.057 (1.011, 1.105)
WPR B-Multi city Korea	8 Korean cities	Son	2013	lag 0	2003-2008	•	1.017 (1.000, 1.035)
WPR B-Single city China China China	Chongqing Hefei Hong Kong	Ding Zhang Ko	2017 2019 2007	best lag lag 0-3 lag 0-4	2013 2015-2016 2000-2005	<u> </u>	1.168 (1.011, 1.350) 1.260 (1.151, 1.379) 1.039 (1.028, 1.050)
Pooled Estimate						0.9 0.95 1 1.05 1.1	1.039 (1.015, 1.064)

Figure S4 Forest plot with study characteristics and individual and pooled epidemiological estimates for the NO_2 effects on asthma hospital admissions in adults (15-64 years old).

WHO Region/ Country	City	Author	Year	Lag	Study period		RR (95% CI) per 10 µg/m3 NO2
EUR A-Multi city Europe	4 European cities	Sunyer	1997	lag 0 up to 3	1986-1992	•	1.006 (1.001, 1.011)
EUR A-Single city	Rome	Michelozzi	2000	lag 0	1995-1997	•	1.024 (0.991, 1.058)
WPR A-Single city Australia	Sydney	Morgan	1998	lag 0	1990-1994	•	1.013 (0.982, 1.045)
WPR B-Multi city Korea	8 Korean cities	Son	2013	lag 0	2003-2008	-	0.989 (0.969, 1.010)
WPR B-Single city China China	Hong Kong Shanghai	Ko Cai	2007 2014	lag 0-4 lag 0-1	2000-2005 2005-2011	-	1.018 (1.007, 1.029) 1.026 (1.012, 1.041)
Pooled Estimate						0.9 0.95 1 1.05 1.1	1.007 (1.000, 1.015)

6.3. Appendix 3: Asthma outcomes for local authorities

Table S1 Central estimate asthma admissions in London from NO_2 air pollution down to cut-off levels – burden from lower end of range of concentrations in health studies to current 2016 levels of pollution.

Local authority	Asthma admissions	Asthma admissions	Asthma/COPD
	0-14	15-64	admissions 65+
City of London	0	<10	<10
Barking and Dagenham	30	<10	36
Barnet	25	<10	39
Bexley	20	<10	32
Brent	43	12	43
Bromley	20	<10	35
Camden	20	<10	39
Croydon	68	13	48
Ealing	43	13	52
Enfield	35	<10	34
Greenwich	44	<10	31
Hackney	33	<10	32
Hammersmith and Fulham	<10	<10	42
Haringey	22	<10	29
Harrow	27	<10	26
Havering	13	<10	39
Hillingdon	26	10	39
Hounslow	23	<10	45
Islington	26	11	46
Kensington and Chelsea	<10	<10	27
Kingston upon Thames	12	<10	15
Lambeth	47	13	48
Lewisham	42	<10	37
Merton	22	<10	26
Newham	57	15	43
Redbridge	40	<10	35
Richmond upon Thames	14	<10	18
Southwark	47	13	57
Sutton	14	<10	24
Tower Hamlets	38	10	53
Waltham Forest	42	<10	36
Wandsworth	26	<10	43
Westminster	18	<10	31

Exact numbers not reported in some Local Authorities due to small number suppression

Table S2 Central estimate asthma admissions in London from NO_2 air pollution down to cut-off levels – burden from lower end of range of concentrations in health studies to current 2019 levels of pollution

Local authority	Asthma admissions 0-14	Asthma admissions 15-64	Asthma/COPD admissions 65+
City of London	<10	<10	<10
Barking and Dagenham	21	<10	22
Barnet	15	<10	29
Bexley	11	<10	27
Brent	31	<10	38
Bromley	11	<10	23
Camden	16	<10	32
Croydon	34	<10	30
Ealing	24	<10	38
Enfield	24	<10	27
Greenwich	20	<10	27
Hackney	24	<10	24
Hammersmith and Fulham	12	<10	27
Haringey	19	<10	20
Harrow	15	<10	25
Havering	<10	<10	26
Hillingdon	26	<10	28
Hounslow	19	<10	33
Islington	14	<10	34
Kensington and Chelsea	<10	<10	19
Kingston upon Thames	13	<10	13
Lambeth	26	<10	34
Lewisham	32	<10	27
Merton	15	<10	18
Newham	40	12	29
Redbridge	28	<10	25
Richmond upon Thames	11	<10	16
Southwark	30	<10	39
Sutton	11	<10	22
Tower Hamlets	36	<10	39
Waltham Forest	41	<10	28
Wandsworth	17	<10	31
Westminster	15	<10	24

Exact numbers not reported in some Local Authorities due to small number suppression

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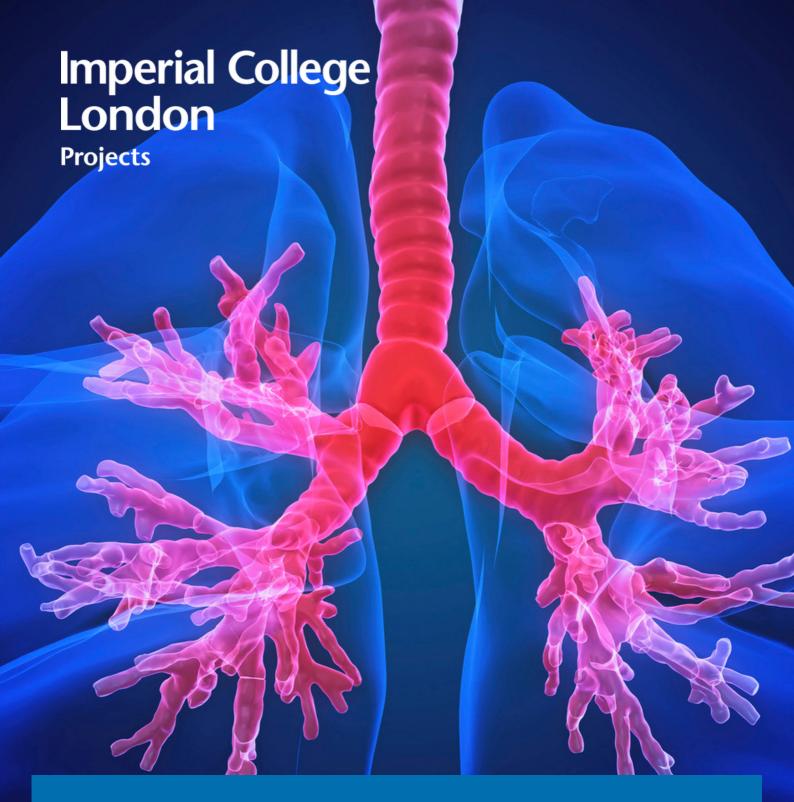
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