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# **Environmental Pollution**



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# The effects of exposure to NO<sub>2</sub>, PM<sub>2.5</sub> and PM<sub>10</sub> on health service attendances with respiratory illnesses: A time-series analysis<sup> $\ddagger$ </sup>

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### ABSTRACT

The associations of exposure to air-pollutants and respiratory illness remains inconsistent and studies have not adequately addressed the non-linearity and delayed effects of exposure. This is a retrospective cohort study using linked routine health and pollution data collected between January 2018 and December 2021. Participants were patients who visited General Practice (GP) or accident and emergency (A&E) services for respiratory illness. Time-series analysis, distributed lagged models, was used to address the potential non-linearity and delayed effects of exposure. There were 114,930 GP and 9878 A&E respiratory visits. For every 10  $\mu$ g/m<sup>3</sup> increase in NO<sub>2</sub> and PM2.5 above the WHO recommended 24-hr thresholds, the immediate relative risk of GP respiratory visits was 1.09 (95% CI: 1.07 to 1.05) and 1.06 (95% CI: 1.01 to 1.10), respectively. The respective relative risk of A&E visit was 1.10 (95% CI: 1.07 to 1.14) and 1.07 (95% CI: 1.00 to 1.14). Exposure to 10-unit increases in NO<sub>2</sub>, PM<sub>2.5</sub> and PM<sub>10</sub> above the WHO recommended 24-hr thresholds, was associated with lagged relative risks of 1.49 (95% CI: 1.42 to 1.56), 5.26 (95% CI: 4.18 to 6.61) and 2.32 (95% CI: 1.66 to 3.26), respectively, for GP respiratory attendances. The lagged relative risk of A&E respiratory visits for same units of exposure in NO<sub>2</sub>, PM<sub>2.5</sub>, and PM10 at the peak lag days were 1.98 (95% CI: 1.82 to 2.15), 4.52 (95% CI: 3.37 to 6.07) and 3.55 (95% CI: 1.85 to 6.84). A third of GP and half of A&E respiratory visits were attributable to exposure to NO<sub>2</sub> beyond the WHO threshold. The combined cost of these visits over the study period was 1.95 million (95% CI: 1.82 to 2.09). High pollution events are related to increased health service use for respiratory illness, with impacts persisting up to 100 days post exposure. The burden of respiratory illness related to air-pollution may be considerably higher than previously reported.

#### 1. Introduction

Air pollution refers to the contamination of the environment by chemical or biological agents that can affect the quality of the air that human and other living beings breathe (World Health Organisation, 2022). The World Health Organisation (WHO) recognises carbon monoxide (CO), particulate matter with aerodynamic diameter of less than 2.5  $\mu$ m (PM<sub>2.5</sub>) and less than 10  $\mu$ m (PM<sub>10</sub>), nitrogen dioxide (NO<sub>2</sub>), ozone (O<sub>3</sub>), and sulphur dioxide (SO<sub>2</sub>) as the major air pollutants of concern for human health (World Health Organisation, 2022).

It is estimated that air pollution causes around 7 million deaths every year, and is such the biggest contributor to environment health risk (World Health Organisation, 2018). The economic cost of exposure to air pollution is also significant—the cost of deaths in Europe alone amounts to \$1.6 trillion per year (United Nations, 2015). In the UK, around 64, 000 deaths occur every year (Lelieveld et al., 2019) which could be costing the country £66 billion a year (World Health Organisation, 2010). As such, the WHO has set out guidelines on air quality levels, based on daily mean air pollutant concentrations and annual time (World Health Organisation, 2021).

The effect of air pollution exposure on respiratory illness has been studied previously (Orellano et al., 2017; Park et al., 2021; Huang et al., 2022). However, results have remained inconsistent. Moreover, the effects investigated by the past studies have been largely instantaneous

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and lagged effects of air pollution exposure have not been adequately considered. Further, excess risk (attributable risk) and number of excess cases (attributable number of illnesses) have also not been reported; meaning extrapolation of health service use was difficult.

Although conventional approaches (i.e. investigating instantaneous effects) can inform us about the relationship between intensity of air pollutant exposure and health outcomes at the point of observation, it does not address the potential delayed effect of exposure on outcomes (Gasparrini and Leone, 2014). In fact, exposure to air pollution 'today' may have health impacts in later days, which is not addressed by the conventional modelling approaches. It is important to study these lagged effects in order to understand how patterns of healthcare use might be impacted by pollution episodes in the days and weeks after an event. Hence, there is a need to use advanced modelling techniques that accommodate the exposure-time (lag) response relationship when investigating the effect of air pollution on respiratory illness and health service use (Gasparrini et al., 2010; Gasparrini, 2014).

The aim of the project was, therefore, twofold: 1) to quantify the instantaneous and lagged effects of air pollution exposure on General Practice (GP) and accident and emergency (A&E) visits for respiratory illness and 2) to estimate the excess risk and total number of GP and A&E visits for respiratory illness along with health service use which helps to understand the number of respiratory visits and costs avoided if measures were taken to reduce air pollution.

#### 2. Methods and materials

#### 2.1. Study design and setting

This is a retrospective population based cohort study using primary care and A&E data. Bradford is the seventh largest metropolitan district in England and Wales with a population of around half a million (Office of National Statistics, 2022). Fifty-seven percent of the population are of White British origin and 26% are of Pakistani origin (Bradford Metropolitan District Council (BMDC), 2021). The city is among the most deprived cities in the UK (Bradford Metropolitan District Council (BMDC), 2019) and has higher morbidity from respiratory illness than the national average (Mebrahtu, 2015; Mebrahtu et al., 2015, 2016). In 2018 it was identified as having illegal levels of pollution in several areas of the city (McEachan et al., 2022).

#### 2.2. Study population

Participants of the study were patients who visited general practice (GP) physician in Bradford metropolitan district and the Bradford Royal Infirmary hospital accident and emergency (A&E) service between January 01, 2018 and December 31, 2021. The start and end dates of the study period were selected based on availability of air pollution data from Bradford city Council.

#### 2.3. Data source

Anonymised GP and A&E patient visits data were obtained from Connected Bradford database at the Bradford Institute for Health Research (Sohal et al., 2022) accessed through Google cloud computing service which were then extracted and harmonised before analysis by one of the authors (TFM). Data on air pollutants (NO<sub>2</sub> and PM<sub>2.5</sub> and PM<sub>10</sub>) were collected by the Bradford City council at six real-time monitoring sites. Fig. S1 details the location map of the sites. All sites provided NO<sub>2</sub> measurements, but only three of the six collected PM<sub>2.5</sub> and PM<sub>10</sub> (Table S1). The Sensors recorded hourly measurements which were quality checked, validated and ratified (Department of Environment Foof and Rural Affairs (DEFRA), 2017), then daily mean concentrations across the sites were calculated for each air pollutant.

#### 2.4. Variables considered

Outcomes were daily number of visits due to respiratory illness in GP and A&E services confirmed by Clinical Terms Version 3 (CTV3) Read codes and ICD10 codes, respectively. Table S2 details the list of codes used to extract GP and A&E visits. Exposure variables considered for analysis were daily mean concentrations of NO<sub>2</sub>, PM<sub>2.5</sub> and PM<sub>10</sub>.

#### 2.5. Statistical analysis and software

First, the daily air pollutant concentrations (NO<sub>2</sub>, PM<sub>2.5</sub> and PM<sub>10</sub>) and GP and A&E visits due to respiratory illnesses were descriptively summarised. To account for non-linearity and the delayed effect of exposure to air pollution on GP and A&E respiratory visits, Distributed Lag Non-linear Models (DLNMs) were used (Gasparrini et al., 2010). Modelling was carried out in two stages. First, DLNMs with a maximum lag time of 60–110 days were fit for each of three air pollutants for exploration. The selection of the maximum lag for each pollutant was guided by the shape or trend of the cumulative effect graphs. A maximum of seven days (one week) was used initially. However, the cumulative effect did not level-off so the lag times were increased gradually until a point where the effect peaked and levelled-off or showed a downward pattern afterwards.

Second, immediate (instantaneous) effect (at lag 0) and delayed (lagged) effects of air pollutants on GP and A&E respiratory attendances were analysed and presented.

Linearity of the lag effect was checked by comparing the Residual deviance values of the non-linear and linear models. Non-linear models (that is, cubic polynomial functions) performed better than the linear so were adopted in the subsequent analyses. The exposure variables were modelled as thresholds (NO<sub>2</sub> =  $25 \ \mu g/m^3$ ; PM<sub>2.5</sub> =  $15 \ \mu g/m^3$ ; PM<sub>10</sub> =  $45 \ \mu g/m^3$ ) based on the WHO global 24-hr air quality guideline (World Health Organisation, 2021).

The instantaneous and lagged dose response and cumulative associated risks of respiratory visits per 10-unit increase above the thresholds were derived along the attributable/excess risks (attributable fraction) and number of cases (attributable number) (Gasparrini and Leone, 2014). Confidence intervals of excess risks and excess number of cases were derived from empirical random samples of 10,000 using Monte Carlo simulation (Greenland, 2004).

The distributed lag equation adopted for deriving Relative Risks (RR) in our analyses was as follows (Almon, 1965):

$$Y_{t} = \sum_{i=0}^{n-1} w(i) X_{t-i}$$
(1)

Where Y is the outcome (dependent) variable, X is the exposure (independent), n is number of cases, w(i) is the weights with which present and past values are combined.

The attributable fraction and attributable numbers were derived using eq. (2) and eq. (3), respectively (Gasparrini and Leone, 2014).

$$AF = 1 - \exp\left(-\sum_{l=l_0}^{L} \beta x_{t-l^{l}}\right)$$
(2)

$$AN = AF_{x,t} * n_t$$
(3)

where AF and AN are attributable fraction and attributable number respectively;  $n_t$  is cases at time t; L is the lag.

Health service use in primary care and A&E services was estimated by multiplying the total number of excess number of visits by the estimated cost of a visit (that is, £39.23 per GP visit and £77 per A&E visit) in National Health Service (NHS) England (The King's Fund, 2022).

All models were adjusted for time (daily), month, day of the week and a binary variable indicating whether a COVID-19 lockdown (where people were encouraged to stay at home, and non-essential shops and services were closed) was in place.

The COVID-19 lockdown indicator variable was a binary where the values were "1" for the three lockdown periods in England and "0" for the rest of the study period. The three lockdown periods were: 1) March 26, 2020 to May 31, 2020, 2) November 05, 2020 to December 02, 2020, and 3) January 06, 2021 to March 08, 2021 (Institute for Government, 2022).

A 5% significance level and 95% confidence intervals were adopted throughout. All analyses were conducted in R software (Version 4.2.0), using 'dlnm' r-package (Gasparrini, 2011).

#### 2.6. Ethics approval

Ethical approval for Connected Bradford was granted from the NHS East Midlands – Derby Research Ethics Committee (Ref: 17/EM/0254 and 22/EM/0127).

#### 3. Results

#### 3.1. Descriptive summary

There were a total of 114,930 GP and 9878 A&E visits due to respiratory illnesses during the four year study period, with daily visits peaking during winter months (November–February). GP and A&E visits declined during the UK COVID-19 lockdown months (e.g. March–May 2020). The daily mean air pollutant concentrations showed the same pattern as the respiratory visits, with peaks during the winter months. See Fig. 1 and Table S3.

The daily mean NO<sub>2</sub>, PM<sub>2.5</sub> and PM<sub>10</sub> concentrations were higher, close to and lower than their respective WHO maximum recommended values (NO<sub>2</sub> = 25  $\mu$ g/m<sup>3</sup>, PM<sub>2.5</sub> = 15  $\mu$ g/m<sup>3</sup> and PM<sub>10</sub> = 45  $\mu$ g/m<sup>3</sup>) for majority of the follow-up days. Amongst the four follow-up years, the

highest pollution concentration recorded was between December 2018 and February 2019, where the daily concentration of the air pollutants (PM<sub>2.5</sub> and PM<sub>10</sub>) recorded was as high as 80  $\mu$ g/m<sup>3</sup>. See Fig. 1 and Table S4 for details.

#### 3.2. Effects of air pollutants on respiratory visits

#### 3.2.1. Instantaneous effects

Exposure to only two of the three pollutants (NO<sub>2</sub> and PM<sub>2.5</sub>) was associated with statistically significant instantaneous effect on GP respiratory visits for exposure of 10  $\mu$ g/m<sup>3</sup> above the WHO thresholds. The relative risk of attending a GP on the same day due to exposure to NO<sub>2</sub> and PM<sub>2.5</sub> was 1.09 (95% CI: 1.07 to 1.11) and 1.06 (95% CI: 1.01 to 1.10), respectively. In contrast, the instantaneous relative risk for PM<sub>10</sub> was 1.03 (95% CI: 0.94 to 1.13), see Table 1. The instantaneous relative risks for exposure to NO<sub>2</sub> and PM<sub>2.5</sub> increased as the doses increased (see Fig. 2).

There was a significant excess risk of GP respiratory visits due to NO<sub>2</sub> exposure (attributable risk = 10.1%, 95% CI: 8.0 to 12.2). The excess risk for PM<sub>2.5</sub> exposure was also marginally significant (attributable risk = 0.6%; 95% CI: 0.1 to 1.1) but not so for PM<sub>10</sub> (attributable risk = 0.05%; 95% CI: 0.0 to 0.2). The respective attributable number of GP respiratory visits due to NO<sub>2</sub>, PM<sub>2.5</sub> and PM<sub>10</sub> were 11,647 (95% CI: 9189 to 14,007), 727 (95% CI: 158 to 1256) and 61 (95% CI: 0 to 234) over the four year period. See Table 1 for further details.

Similar patterns of relative risks, excess risks and excess number of cases were observed for A&E respiratory visits. See Table 1 and Fig. 2 for details.

#### 3.2.2. Lagged effects

Exposure to the three air pollutants was associated with a significant delayed effect on GP respiratory visits with steady increase until the



Fig. 1. Daily mean concentrations of air pollutants and GP visits due to respiratory illnesses (horizontal dotted lines are of WHO 24-hr thresholds and vertical dotted lines are national UK COVID-19 lockdown periods).

#### Table 1

Instantaneous effects of air pollutants on respiratory visits for 10  $\mu$ g/m<sup>3</sup> dose beyond WHO 24-hr mean threshold.

	RR (95% CI)	AR (95% CI)‡*	AN (95% CI)‡*
GP Visits			
$NO_2$ (threshold = 25	1.09	10.1% (7.9–12.2)	11,647 (9189 to
μg/m <sup>3</sup> )	(1.07 - 1.11)		14,007)
$PM_{2.5}$ (threshold =	1.06	0.6% (0.1–1.1)	727 (158–1256)
15 μg/m <sup>3</sup> )	(1.01 - 1.10)		
$PM_{10}$ (threshold =	1.03	0.05% (0.0–0.2)	61 (0–234)
45 μg/m <sup>3</sup> )	(0.94–1.13)		
A&E Visits			
$NO_2$ (threshold = 25	1.10	10.2% (7.3–12.9)	1009 (732–1269)
μg/m <sup>3</sup> )	(1.07 - 1.14)		
$PM_{2.5}$ (threshold =	1.07	0.7% (0.01–1.4)	74 (1–140)
15 μg/m <sup>3</sup> )	(1.00-1.14)		
$PM_{10}$ (threshold =	0.91	-0.01% (-0.04	-11 (-44 to 10)
45 μg/m³ <b>)</b>	(0.76 - 1.10)	to 0.01)	

Note: AN, attributable number; AR, attributable risk; CI, confidence intervals; NO<sub>2</sub>, nitrogen dioxide; PM, particulate matter; RR, relative risk;  $\ddagger$ , combined effect of all doses; \*, confidence intervals derived from empirical random samples of 10,000; AN; AR and RR values are cumulative for every dose increase beyond the thresholds.

peak lag days (NO<sub>2</sub> = 55days; PM<sub>2.5</sub> = 100 days and PM<sub>10</sub> = 35days), see Fig. 3. For every 10 unit above the '24-hr mean' WHO threshold of NO<sub>2</sub>, PM<sub>2.5</sub> and PM<sub>10</sub>, the peak lag day's relative risk was 1.49 (95% CI: 1.42 to 1.56), 5.26 (95% CI: 4.18 to 6.61) and 2.32 (95% CI: 1.66 to 3.26), respectively. The respective cumulative excess risk of GP respiratory visits, at the peak lag days, were 35.0% (95% CI: 31.8 to 37.9), 17.0% (95% CI: 15.0 to 18.9) and 1.4% (0.9–2.0). The associated number of excess GP visits (for a 10 unit increase above WHO thresholds up to the peak lag days) in NO<sub>2</sub>, PM<sub>2.5</sub> and PM<sub>10</sub> were 40,174 (36,490 to 43,532),

19,528 (17,168 to 21,721) and 1659 (1002 to 2222), respectively, see Table 2. The associated relative risks due to pollution exposure increased as the dose increased. See Fig. 3 for further details.

The peak lag days for NO<sub>2</sub>, PM<sub>2.5</sub> and PM<sub>10</sub> in A&E respiratory visits were 87 days, 76 days and 58 days, respectively, see Fig. 4. The relative risks of A&E respiratory visits for the exposure to higher than the '24-hr mean' by 10 units for NO<sub>2</sub>, PM<sub>2.5</sub>, and PM<sub>10</sub> at the peak lag days were 1.98 (95% CI: 1.82 to 2.15), 4.52 (95% CI: 3.37 to 6.07) and 3.55 (95% CI: 1.85 to 6.84), See Table 2.

# 3.3. Health service use cost

At the lag time where the cumulative effect peaked (day 55), the cumulative costs attributable to NO<sub>2</sub> exposure were £1,576,026 (95% CI: 1,431,502.7 to 1,707,760.36). At their respective 'peak lag' days (day 100 and day 35) the cumulative attributable cost due to exposure to PM<sub>2.5</sub> and PM<sub>10</sub> were £766,083.44 (95% CI: 673,500.64 to 852,114.83) and £65,082.57 (95% CI: 39,308.46 to 87,169.06), respectively.

The estimated cumulative attributable costs of A&E service due to exposure to NO<sub>2</sub>, PM<sub>2.5</sub> and PM<sub>10</sub> were £379,456 (95% CI: 348,117 to 406,945), £115,962 (95% CI: 96,019 to 133,980) and £15,785 (7546 to 22,792), respectively.

Using a conservative estimate where there is a complete overlap amongst the number of visits due to the NO<sub>2</sub>, PM<sub>2.5</sub> and PM<sub>10</sub>, the total health services cost for respiratory illness due to pollution levels 10  $\mu$ g above thresholds, in district with a population of half a million was calculated to be £1,955,482.02 over 4 years (95% CI: 1,820,910.18 to 2,090,053.87).



Note: A&E, accident and emergency; CI, confidence interval; GP, General Practice; grey areas are of 95% CIs.

Fig. 2. Instantaneous effects and 95% CI of air pollutant exposure on GP and A&E respiratory visits Note: A&E, accident and emergency; CI, confidence interval; GP, General Practice; grey areas are of 95% CIs.

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Note: GP, General Practice; NO<sub>2</sub>, nitrogen dioxide; PM, Particulate Matter; RR, relative risk; WHO, World Health Organisation.

Fig. 3. Cumulative relative risk of GP respiratory visits for selected air pollutant concentrations above 24-hr mean WHO thresholds Note: GP, General Practice; NO<sub>2</sub>, nitrogen dioxide; PM, Particulate Matter; RR, relative risk; WHO, World Health Organisation.

#### Table 2

Associated risk of respiratory illness for 10 unit increase of air pollutants above the 24-hr mean thresholds at peak lag days.

	RR (95% CI)	AR (95%CI) ‡	AN (95%CI) ‡
GP visits			
$NO_2$ (threshold = 25 µg/	1.49	35.0%	40,174 (36,490 to
m <sup>3</sup> ; lag 55)	(1.42 - 1.56)	(31.8-37.9)	43,532)
$PM_{2.5}$ (threshold = 15	5.26	17.0%	19,528 (17,168 to
µg/m <sup>3</sup> ;lag 100)	(4.18-6.61)	(15.0–18.9)	21,721)
$PM_{10}$ (threshold = 45	2.32	1.4% (0.9–2.0)	1659 (1002 to
μg/m <sup>3</sup> ; lag 35)	(1.66 - 3.26)		2222)
A&E visits			
$NO_2$ (threshold = 25 µg/	1.98	49.9%	4928 (4521 to
m <sup>3</sup> ; lag 87)	(1.82 - 2.15)	(45.8–53.6)	5285)
$PM_{2.5}$ (threshold = 15	4.52	15.2%	1506 (1247 to
μg/m³; lag 76)	(3.37-6.07)	(12.7–17.7)	1740)
$PM_{10}$ (threshold = 45	3.55	2.1% (1.0-3.0)	205 (98–296)
μg/m <sup>3</sup> ; lag 58)	(1.85-6.84)		

Note: AN, attributable number; AR, cumulative attributable risk;  $NO_2$ , nitrogen dioxide; PM, particulate matter; RR, relative risk;  $\ddagger$ , confidence intervals derived from empirical random samples of 10,000; AN, AR and RR values are cumulative for every dose increase beyond the thresholds and every lag until the peak lag time.

#### 4. Discussion

We explored relationships between exposure to NO<sub>2</sub>,  $PM_{2.5}$  and  $PM_{10}$  with health care service use for respiratory illness over four years. We found that exposure to NO<sub>2</sub> and  $PM_{2.5}$  had an immediate impact on GP and A&E attendances which is evidenced in the relative risk, excess risk and attributable number of illness estimates per units of dose increase in the pollutants. For example, every 10 µg/m<sup>3</sup> of NO<sub>2</sub> beyond the WHO

24-hr mean threshold was associated with a 10% excess risk of GP and A&E attendances. The delayed effect of exposure to the three pollutants (NO<sub>2</sub>, PM<sub>2.5</sub> and PM<sub>10</sub>) was also considerably high. For example, every 10  $\mu$ g/m<sup>3</sup> of NO<sub>2</sub> beyond the WHO threshold was associated with cumulative attributable risks 35% of GP and 50% of A&E respiratory visits at their peak lag period.

Our analyses indicated that exposure to PM10 was not related with increase in respiratory visits at the point of observation (that is, instantaneous or immediate effect). This could be due to two main reasons. First, it could mean that PM10 does not have immediate effect on health but rather have only a delayed effect. Second, it could also mean that the current WHO 24-hr threshold for PM10 is too high. For example, when we did further exploration of thresholds, we found out that only if the threshold was lowered from 45  $\mu$ g/m<sup>3</sup> to 15  $\mu$ g/m<sup>3</sup> an immediate effect on respiratory visits would be apparent. For every 10-unit above 15  $\mu$ g/m<sup>3</sup>, the relative risks of GP respiratory visits and A&E visits were 1.04 (1.01–1.07) and 1.05 (95% CI: 1.01 to 1.09), respectively. If this is confirmed by further studies, it could mean that the current WHO 24-hr mean for PM<sub>10</sub> may need to be lowered to around 15  $\mu$ g/m<sup>3</sup>.

The instantaneous effect of exposure to air pollution on respiratory health has been reported to be inconsistent by previous studies (Liu et al., 2017; Doiron et al., 2019; Park et al., 2021; Salimi et al., 2022). In a meta-analysis of five studies (Park et al., 2021), a 10  $\mu$ g/m<sup>3</sup> increase in the exposure of NO<sub>2</sub> (Hazard Ratio (HR) = 1.07; 95% CI: 1.00 to 1.16) and PM<sub>2.5</sub> (HR = 1.18; 95% CI: 1.13 to 1.23) was associated with increased incidence of chronic obstructive pulmonary disease (COPD), whilst a 10  $\mu$ g/m<sup>3</sup> increase in PM<sub>10</sub> (HR = 0.95; 95% CI: 0.83 to 1.06) appeared to be associated with a reduction of COPD, albeit non-significant. In another cohort study, an increase of 10  $\mu$ g/m<sup>3</sup>, 5  $\mu$ g/m<sup>3</sup> and 10  $\mu$ g/m<sup>3</sup> in NO<sub>2</sub> (Odds Ratio (OR) = 1.05; 95% CI: 0.89 to



Note: A&E, Accident and Emergency; PM, Particulate Matter; RR, relative risk; WHO, World Health Organisation.

Fig. 4. Cumulative relative risk of A&E respiratory visits for selected air pollutant concentrations above 24-hr mean WHO thresholds Note: A&E, Accident and Emergency; PM, Particulate Matter; RR, relative risk; WHO, World Health Organisation.

1.23),  $PM_{2.5}$  (OR = 1.06; 95% CI: 0.73 to 1.53) and  $PM_{10}$  (OR = 1.10; 95% CI: 0.70 to 1.73), respectively, was not related with significant increase in the incidence of COPD (Schikowski et al., 2014). Further, two other studies reported increased prevalence of COPD with increased exposure to NO<sub>2</sub>,  $PM_{2.5}$  and  $PM_{10}$  (Liu et al., 2017; Doiron et al., 2019) and another one reported of no significant effect of exposure to NO<sub>2</sub> and  $PM_{2.5}$  on respiratory admissions (Salimi et al., 2022).

In a recent meta-analysis of 27 studies (Huang et al., 2022), an increase of 10  $\mu$ g/m<sup>3</sup> in the three air pollutants (NO<sub>2</sub>, PM<sub>2.5</sub> and PM<sub>10</sub>, separately) was associated with an increased risk of asthma exacerbations by 1% (RR = 1.01; 95% CI: 1.01 to 1.01). In our study, we found significant increases of GP and A&E respiratory visits for every increase of 10  $\mu$ g/m<sup>3</sup> beyond the WHO thresholds in NO<sub>2</sub> and PM<sub>2.5</sub> but not so for PM<sub>10</sub>. However, it must pointed out that we have used a broader outcome definition and advanced modelling approach to account the effect of exposure beyond WHO recommended maximum thresholds which was not used by the other studies.

A lagged effect of exposure to air pollution on respiratory illness has been investigated previously. However, the duration of the lag time considered was short (one day) and the effects of the lag and exposure doses were assumed to be linear which may not necessarily be the case. Nonetheless, a recent meta-analysis of 24 studies reported that an increase of 10  $\mu$ g/m<sup>3</sup> in the three air pollutants (NO<sub>2</sub>, PM<sub>2.5</sub> and PM<sub>10</sub>) was associated with a marginal lagged increase of risk of asthma exacerbations (RR = 1.01; 95% CI: 1.00 to 1.01) after one day of exposure (Huang et al., 2022). In a recent study that used a similar modelling approach to ours but compared higher (95th) with lower (25th) percentile of exposure (Yang et al., 2022), there was no significant lagged increase in pneumonia hospital visits in 95th percentile doses when compared with 25th percentile doses of NO<sub>2</sub>,PM<sub>2.5</sub> and PM<sub>10</sub> after 6 days (lag days) of exposure. Using the WHO cut-off values as thresholds, our study has found significant lagged effect of the three pollutants for doses higher than the WHO thresholds, which contradicts these previous findings. When we also compared the 95th percentile and 25th percentile exposure doses at 6 days lag in our study, there was an increase of GP respiratory visits for NO<sub>2</sub> (RR = 1.59, 95% CI: 1.42 to 1.77), PM<sub>2.5</sub> (RR = 1.43, 95% CI: 1.30 to 1.57) and PM<sub>10</sub> (RR = 1.29, 95% CI: 1.17 to 1.43). The relative risks of A&E respiratory visits for the same comparisons of NO<sub>2</sub>, PM<sub>2.5</sub> and PM<sub>10</sub> were 1.95 (95% CI: 1.66 to 2.29), 1.79 (95% CI: 1.57 to 2.05) and 1.48 (95% CI: 1.28 to 1.71).

Our study has a number of strengths. First, we have used a large sample size for our analysis studying more than 120,000 respiratory visits over a four year period. Second, we were able to explore health care usage across both primary (general practice) and secondary (emergency attendance) modalities. Third, we used electronic health records data minimising the inherent biases and errors in other types of observational data. Finally we have implemented advanced statistical modelling technique to address the lagged effects and potential nonlinearity of air-pollution exposure and explored lags over longer periods to get a fuller understanding of the impact of pollution on health service use. Nonetheless, our study has some weaknesses. First, although minimal, errors during data entry and processing prior to our receipt of the electronic health records and air pollution data cannot be ruled out. Second, we have assumed that every respiratory illness patient had presented themselves to their GP or A&E which may not be the case, meaning the total impact of pollution may be higher than reported. Third, A&E data was available only from one of the two hospitals in the district which may not be representative of the two hospitals and that our A&E estimated costs may not reflect for all A&E visits in the district. Fourth, although we have adjusted our models for a group of timevarying factors, a presence of other unaccounted factors cannot be ruled out. Fifth, it has been assumed that people who used the GP and A&E services were residents of Bradford metropolitan district. Sixth, our study was located in an urban, deprived city, with high levels of health needs and may not be reflective of other areas in the UK. Further, the calculated daily mean concentrations of  $PM_{2.5}$  and  $PM_{10}$  were based on only three sites so may not be representative of the Bradford district air pollutant concentrations.

#### 5. Conclusion

The impact of exposure to air pollution on respiratory illness, assessed by visits to GP and A&E settings is considerable. High levels of exposure (that is, exposure levels above the WHO 24-hr mean thresholds) lead to increased pressure on health care services that can persist up to 100 days after an exposure event. Taking these delayed effects on service use into account, it is estimated that up to 50% of emergency health care and 35% of general practice respiratory illness visits may be caused by high levels of pollution, leading to a substantial financial burden to healthcare providers. Our findings are of value to health care providers to understand the length of time in which increased health service use might be apparent after air pollution episodes. Effective tracking of air quality levels about WHO recommended 24-hr mean estimates will be important to identify periods of peak demand. However, given the substantial health and societal impact of pollution the implementation of policies at a city scale to reduce air pollution are warranted.

#### Authors' contribution

TM: Conceptualisation, methodology, formal analysis, data curation, writing-original draft, writing—review & editing, project administration—manage day-to-day research related activities, GS: Conceptualisation, data curation, writing—review & editing, funding acquisition, TY: Conceptualisation, writing—review & editing, project administration, funding acquisition, JW: Writing—review & editing, funding acquisition, JT: Writing—review & editing, funding acquisition, writing—review & editing, funding acquisition, writing—review & editing, funding acquisition, JT: Writing—review & editing, funding acquisition, review & editing, funding acquisition, review & editing, funding acquisition, writing—review & editing, funding acquisition, review & editing, funding acquisition, review & editing, funding acquisition, funding acquisition, writing—review & editing, project administration, funding acquisition.

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#### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper

#### Data availability

The data that has been used is confidential.

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#### Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envpol.2023.122123.

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