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Traffic-related air pollution and the local burden of childhood asthma in Bradford, UK

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ABSTRACT

Asthma is a burdensome disease which is often cited as the most common chronic disease in childhood. Traffic-related air pollution (TRAP) may be an important exposure in the development of childhood asthma. However, the burden of childhood asthma attributable to TRAP is poorly documented. Using a land-use regression (LUR) model, we estimated the childhood (birth-18 years old) population exposure to the following three air pollutants in Bradford, UK: Particulate Matter equal or less than 2.5 micrometers in diameter ($PM_{2.5}$), Particulate Matter equal or less than 10 micrometers in diameter (PM_{10}) and Black Carbon (BC). We assigned exposures at the lowest census tract level: the 'output area'. We extracted national and local childhood asthma incidence rates from the literature and used meta-analytic exposure-response functions to calculate the relative risk, population attributable fraction of childhood asthma in association with each pollutant and the number of childhood asthma cases attributable to each pollutant. We investigated the impacts of reducing air pollutants at each output area to comply with the World Health Organization's (WHO) air quality guidelines. At the output area level, the annual mean $PM_{2.5}$, PM_{10} and BC concentrations were 10.40 $\mu g/m^3$, 16.63 $\mu g/m^3$ and 1.07×10^{-5} m^{-1}, respectively. Depending on the pollutant, the estimated number of attributable childhood asthma cases varied between 279 and 612 annually, representing between 15% and 33% of all cases in the city. Between 7% and 12% of annual childhood asthma cases were specifically attributable to TRAP. Compliance with the WHO air quality guidelines prevented up to 29 cases. Using national versus local baseline childhood asthma incidence rates with differing underlying asthma definitions resulted in up to 322% as many attributable cases.

Abbreviations: BC, $PM_{2.5\ absorbance}$/black carbon; BoD, Burden of disease; E&W, England and Wales; ESCAPE, European Study of Cohorts for Air Pollution Effects; GIS, Geographical information systems; LUR, Land-use regression; NO_2, Nitrogen Dioxide; NO_x, Nitrogen Oxides; OR, Odds Ratio; PAF, Population attributable fraction; PM_{10}, Particulate Matter equal or less than 10 micrometers in diameter; $PM_{2.5}$, Particulate Matter equal or less than 2.5 micrometers in diameter; RMSE, Root-Mean-Square Error; RR, Relative risk; TRAP, Traffic-related air pollution; UK, United Kingdom; WHO, World Health Organization.

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Air pollution is estimated to cause a large, but preventable, childhood asthma burden. The burden of disease varied depending on the pollutant selected.

1. Background

Asthma is a chronic disorder of the airways affecting more than 334 million people worldwide (Global Asthma Network, 2014), and associated with increased morbidity and mortality (World Health Organization, 2013). Over the past four decades, the prevalence of asthma has been steadily increasing across many regions (Anandan et al., 2010; McCunney, 2005). The condition is often cited as the most common chronic illness of childhood (Gasana et al., 2012; Gaffin and Phipatanakul, 2014; Asher and Pearce, 2014).

The relatively rapid increases in asthma's incidence and prevalence are not fully explained. Whilst hereditary factors are important in asthma's pathogenesis, the rapid rises in prevalence outstrip the pace of genomic variation (Gaffin et al., 2014). As recent increases remain unexplained by genes alone, environmental factors, independently and jointly with genetic factors, are presumably responsible (Clark et al., 2010; Cookson, 2004). In recent years, the number of epidemiological studies investigating various environmental exposures that can modify the risk of asthma has grown substantially. These exposures include, but are not limited to, exposure to domestic pets (Almqvist et al., 2003; Apelberg et al., 2001; Carlsten et al., 2010; Dong et al., 2009), exposure to allergens, including animal, mouse, rat, cockroach, house dust mite, fungal, tree and weed antigens (Arshad, 2010; Arshad et al., 2002; Barnes et al., 2001; Breysse et al., 2010; Byrd and Joad, 2006; Carrer et al., 2001; Chen et al., 2011), exposure to parental and especially maternal tobacco smoke (Gilmour et al., 2006; Gilliland et al., 2001; Arruda et al., 2005; Chen et al., 2011; Chhabra et al., 1999), and exposure to indoor and outdoor air pollution (Belanger and Triche, 2008; Breysse et al., 2010; Khreis et al., 2017). From this list, we focus on exposure to outdoor air pollution.

Until relatively recently, the common wisdom about air pollution and asthma was that air pollution can exacerbate pre-existing asthma across a variety of outcomes such as increasing rates of hospitalizations, emergency room visits, and medication used (Schildcrout et al., 2006; Schwartz et al., 1993; Gauderman et al., 2002; Sunyer et al., 1997; Lierl and Hornung, 2003; Lipsett et al., 1997; Von Klot et al., 2002; Slaughter et al., 2003; Handzel, 2000), but could not lead to the development of the disease (Eder et al., 2006; Committee on the Medical Effects of Air Pollutants, 1995). Numerous studies showed that asthma incidence rates were not higher in communities with higher regional air pollution, supporting this school of thought (McConnell, 2013). A meta-analysis of cross-sectional studies by Anderson et al. (2013), which included 21 studies examining the community level concentrations of multiple air pollutants (nitrogen dioxide, particulate matter, ozone and sulphur dioxide), found no association with asthma prevalence.

In recent years, however, other syntheses examined air pollution concentrations that were associated with traffic and showed positive and statistically significant associations with asthma incidence and prevalence (Health Effects Institute, 2010). The most up-to-date synthesis is the meta-analysis by Khreis and colleagues (2017) in which we examined the associations between exposure to traffic-related air pollution (TRAP) and *subsequent* childhood asthma incidence or lifetime prevalence as quantified in case control, cohort, and cross-sectional studies (Khreis et al., 2017). In this meta-analysis, we included 41 studies and found positive and statistically significant associations between childhood asthma incidence or lifetime prevalence (referred to as childhood asthma development thereafter) and $PM_{2.5\ absorbance}$/Black Carbon (BC), nitrogen dioxide (NO_2), particulate matter equal or less than 2.5 micrometers in diameter ($PM_{2.5}$) and particulate matter equal or less than 10 micrometers in diameter (PM_{10}). We also found a positive but statistically insignificant association between nitrogen oxides (NO_x) and childhood asthma development.

In a recent burden of disease assessment paper, we quantified the public health impacts of the associations between NO_2 and NO_x and childhood asthma development in Bradford, UK (Khreis et al., 2018). We, however, did not quantify the impacts of exposure to the other pollutants for which we have exposure-response functions: $PM_{2.5}$, PM_{10} and BC.

Although there is a general focus on studying the health effects and impacts of NO_2 in the literature (Favarato et al., 2014; Khreis et al., 2017; Cyrys et al., 2003), there is unresolved debate about whether NO_2 is a causal agent (for numerous health outcomes) or simply an indicator of other traffic-related air pollutants and/or the effect of the mixture (Health Effects Institute, 2016). In Europe especially, there is also a focus on NO_2 in air quality guidelines, plans and mitigation strategies, whilst less attention is given to the other pollutants, despite their higher toxicity and potential relevance (Li et al., 2003a,b).

In this paper, we therefore expand previous NO_2 and NO_x estimates and quantify the number of childhood asthma cases attributable to $PM_{2.5}$, PM_{10} and BC in Bradford, UK, and especially the traffic-related component of $PM_{2.5}$, PM_{10} and BC. We then discuss how the final estimates varied depending on the pollutant's selection. We also investigate the health impacts of reducing air pollutants to comply with the World Health Organization's (WHO) air quality guideline values, where these values are being breached.

2. Methods

2.1. Setting

This study was set in Bradford, a city in the North of England, with approximately 534,300 inhabitants (City of Bradford Metropolitan District Council, 2017). In terms of population, Bradford is the fifth largest English metropolitan district (City of Bradford Metropolitan District Council, 2017) and has a different demographic structure when compared to other cities in England and Wales (E&W) with more people under the age of 16 (Bradford has 22.6% whilst E&W have 18.7%) (Fielding, 2012). Further, Bradford is one of the 10% most deprived local authorities in the UK, with significant deprivation discrepancy between the different neighborhoods (Fielding, 2012; Wright et al., 2013).

Bradford has high rates of childhood morbidity and mortality accompanied by rising public concern about the effect of environmental toxins, particularly air pollution, on health (Wright et al., 2013). The recorded prevalence of asthma in Bradford is 6.3% which is higher than both the national (5.9%), and regional (6.2%) averages (Quality and Outcomes Framework, 2012). Data from 2012 indicates that emergency hospital admissions for asthmatics in Bradford were also higher than national and regional averages, with children aged birth to 4 responsible for the highest proportion of admissions (Bradford Joint Strategic Needs Assessment, 2014).

The major sources of air pollution in the district have been identified as regional rural concentrations, traffic, industry, and domestic, institutional and commercial space heating. Less important sources include point sources, rail, and aircrafts (Department for Environment Food and Rural Affairs, 2010).

The work we present in this paper is part of ongoing work in Bradford assessing the emissions and air quality profile in the district and the associated childhood health effects and impacts. The analysis year was 2010: the year when the land-use regression (LUR) model we used was constructed.

2.2. Air quality assessment

We assessed air quality in Bradford using previously established and validated LUR models, which were developed for London/Oxford as part of the European-wide ESCAPE project (European Study of Cohorts for Air Pollution Effects, 2014). The London/Oxford LUR models were assumed to apply to Bradford and were used in this research study, in line with previous publications (Pedersen et al., 2013; Schembari et al., 2015).

In this paper, we focus on exposures to $PM_{2.5}$, PM_{10} and BC in Bradford. A previous paper dealt with the exposures to NO_2 and NO_x (Khreis et al., 2018). In the following paragraphs, we therefore briefly describe the $PM_{2.5}$, PM_{10} and BC LUR models adopted. A full description of their underlying data and development can be found in Eeftens et al. (2012a,b).

The LUR method is an empirical method that uses least squares regression to combine measured air pollution data with geographic information system (GIS)-based predictor data reflecting pollutant sources, to build a prediction model applicable to non-measured locations (Khreis and Nieuwenhuijsen, 2017). The LUR models we adopted were developed using airborne particulate matter measurements at 20 sites across the Thames valley: London, Oxford and smaller towns. The $PM_{2.5}$ and PM_{10} measurements were taken using Harvard impactors whilst the BC calculations were done based $PM_{2.5}$ reflectance measurements from Andersen 37 mm 2 mm pore size Teflon filters (Eeftens et al., 2012b).

All measurements were taken between *26 January 2010* and *18 January 2011*. The measurement sites were classified as regional background (n = 1), urban background (n = 12) and traffic sites (n = 7). At each site, measurements were made for three 14-days periods, with each period representing a different season namely the warm, cold and intermediate season. The measurements were adjusted for temporal variability using measurements obtained from a reference fixed-site monitoring station which was operated all year around (Eeftens et al., 2012b).

The summary statistics of the adjusted measurements made at the 20 sites, and used to build the LUR models, are shown in Table 1. The ratios between traffic and urban background site concentrations were 1.26 for $PM_{2.5}$, 1.33 for PM_{10} and 1.77 for $PM_{2.5}$ absorbance/BC.

The LUR models were developed from these measurements in combination with several GIS variables on traffic characteristics, land use, population density, and topography. The final LUR models for the three pollutants are shown in Table 2. The cross-validation R^2 for the $PM_{2.5}$ model was 0.77; 0.88 for the PM_{10} model and 0.92 for the $BC/PM_{2.5\ absorbance}$ model. The root-mean-square error (RMSE) for the $PM_{2.5}$ model was 1.4 $\mu g/m^3$; 1.5 $\mu g/m^3$ for the PM_{10} model and 0.2×10^{-5} m^{-1} for the $BC/PM_{2.5}$ absorbance model (Eeftens et al., 2012a).

Table 1
Means and overall contrasts (total range/mean) of adjusted annual average concentrations of $PM_{2.5}$, $PM_{2.5}$ absorbance/BC, and PM_{10} in London/Oxford.

Pollutant (unit)	Mean (n)	Range	Range/mean (%)	Ratio (traffic/urban background)
$PM_{2.5}$ ($\mu g/m^3$)	11.2 (20)	7.0–21.2	127%	1.26
PM_{10} ($\mu g/m^3$)	18.6 (20)	12.1–31.2	103%	1.33
$BC/PM_{2.5\ absorbance}$ (10^{-5} m^{-1})	1.6 (20)	0.9–4.7	235%	1.77

Table 2
London/Oxford $PM_{2.5}$, PM_{10}, and $PM_{2.5\ absorbance}$/BC LUR models.

Pollutant	LUR model	Variable definitions	R^2 cross-validation
$PM_{2.5}$	$7.19 + 1.38 \times 10^{-3} \times$ INTMAJORINVDIST + $2.65 \times 10^{-4} \times$ ROADLENGTH_500	**INTMAJORINVDIST** is the product of inverse/inverse squared distance to the nearest major road and the traffic intensity on this road (vehicles·day^{-1} m^{-1}/vehicles day^{-1} m^{-2}) **ROADLENGTH_500** is total length (m) of all road segments in a 500 m buffer	0.77
PM_{10}	11.40 + 76.99*DISTINVMAJORC1 + 1.35E^{-3}*HEAVYTRAFMAJOR + 1.30E^{-5}*HLDRES_30	**DISTINVMAJORC1** is the inverse distance (m^{-1}) and inverse squared distance (m^{-2}) to the nearest major road in the central network **HEAVYTRAFMAJOR** is heavy traffic intensity on the nearest major road **HLDRES_30** is the surface area (m^2) of all residential land within a 30 m buffer	0.88
BC/$PM_{2.5\ absorbance}$	$0.81 + 1.12 \times 10^{-7} \times$ HEAVYTRAFLOAD_500 + $8.00 \times 10^{-9} \times$ HLDRES_5000 + $125.41 \times$ DISTINVMAJORC2	**HEAVYTRAFLOAD_500** is the sum of (traffic intensity × the length of all road segments) within a 500 m buffer (vehicles·day^{-1} m) for heavy traffic **HLDRES_5000** is the surface area (m^2) of all residential land within a 5000 m buffer **DISTINVMAJORC2** is the inverse distance (m^{-1}) and inverse squared distance (m^{-2}) to the nearest major road in the central network	0.92

2.3. Burden of disease assessment

We followed standard procedures to assess the childhood asthma burden of disease (BoD) in association with the three different pollutants ($PM_{2.5}$, PM_{10}, and $PM_{2.5\ absorbance}$/BC) (Perez et al., 2009; World Health Organization, 2015), by:

- defining the exposure measures;
- defining the baseline incidence rate of asthma amongst the exposed children;
- selecting exposure-response functions to quantify the strength of association between the exposures and the development of asthma;
- combining exposures data with population data and the exposure-response functions to quantify the attributable proportional burden of incident childhood asthma cases.

The following paragraphs describe each step and the data sources that we used.

2.3.1. Childhood population and census data

The Census output area is the lowest/smallest geographical census tract in the UK at which census data is provided (Office for National Statistics, 2016). The output area was used as the unit of analysis in this study where we assigned childhood population data (population between birth and 18 years old, as downloaded from the census), exposure data, relative risks, population attributable fractions (PAFs) and attributable number of asthma cases (see next). We used the 2011 census data as these were most compatible with the 2010 LUR models.

The Bradford's output areas are shown in Fig. 1 and their characteristics are described in Table 3. Overall, there were 1528 output areas in which 143,472 children, aged birth to 18 years old, lived. 152 of these output areas, however, had no exposure estimates and hence were excluded from the final analyses, as described next.

2.3.2. Exposure assessment and missing data

The LUR models described above were used to estimate $PM_{2.5}$, PM_{10} and BC at 46,452 specified output points (X, Y pairs) throughout Bradford. Each specified output point was the centroid of a 100 m × 100 m grid/box and all the points combined covered an area of approximately ≈40 * 33 km in Bradford. At each 100 m × 100 m grid, the centroid's $PM_{2.5}$, PM_{10} and BC estimate from the corresponding LUR model was applied to whole 100 m × 100 m grid (i.e. the exposure estimate at the centroid of the 100 m × 100 m grid was given to the whole grid cell). An air pollution (raster) surface was then developed for each pollutant, with a resolution of 100 m × 100 m (Fig. 2). This process was undertaken in ArcMap version 10.4 using the Point to Raster conversion tool.

To assign the exposure for children living in each output area, each output area was intersected with the underlying raster air pollution surfaces, for $PM_{2.5}$, PM_{10} and BC. The 100 m × 100 m underlying raster cell values contained within each census output area were averaged, resulting in one annual average air pollution exposure estimate at each output area. This annual average air pollution exposure estimate was then applied to all children living in the corresponding output area. This process

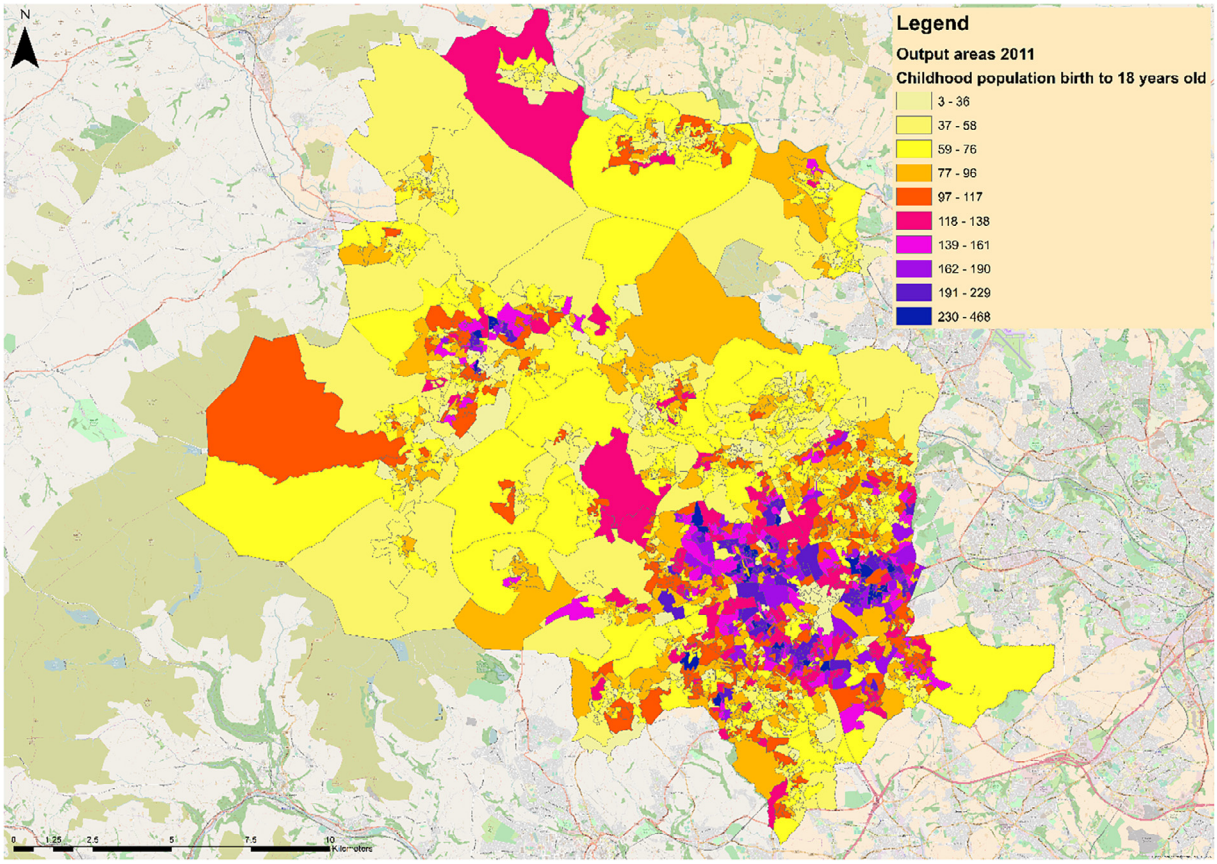

Fig. 1. Bradford's Census Output Areas and Childhood Population.

Table 3
Characteristics of Bradford's Census Output Areas.

Number of total output areas	1528 output areas
Total number of children in all output areas (birth – 18 y.o.)	143,472 children
Output areas excluded	152
Total number of children in excluded output areas (birth – 18 y.o.)	9804 children
Average number of children in all output areas (birth – 18 y.o.)	94 children
Minimum number of children in an output area (birth – 18 y.o.)	3 children
Maximum number of children in an output area (birth – 18 y.o.)	468 children
Average area of all output areas (m^2)	239,802
Minimum area of an output area (m^2)	3817
Maximum area of an output area (m^2)	15,395,650

was undertaken in Geospatial Modelling Environment suite version 0.7.4.0. using the 'isectpolyrst' tool (Intersect Polygons with Raster).

There were 152 output areas where there was no intersection between the air pollution raster surfaces and the output areas' boundaries (Fig. 2.). The reason was that the air pollution raster surfaces covered a lesser extent than the census maps; as some of the necessary GIS-based variables (for example, the traffic characteristics) for the LUR models (Table 2) were unavailable for the whole area covered by the census. These 152 output areas, where 9804 children, or 6.8%, of all children lived, were excluded from our analysis. This exclusion underestimates the overall burden of childhood asthma attributable to $PM_{2.5}$, PM_{10} and BC in Bradford, but does not affect the reported percentage of attributable cases.

2.3.3. Baseline childhood asthma incidence rates

The incidence rate of asthma in children from birth to 18 years old *specific to Bradford* was not found in the peer reviewed or grey literature. Instead, we used the UK's national incidence rate of childhood asthma for the same age group (birth to 18 years old), as reported by Punekar and Sheikh (2009). This equaled *137 clinician-diagnosed asthma cases per 10,000 person-years*, as identified for 43,473 children indexed in the General Practice Research Database.

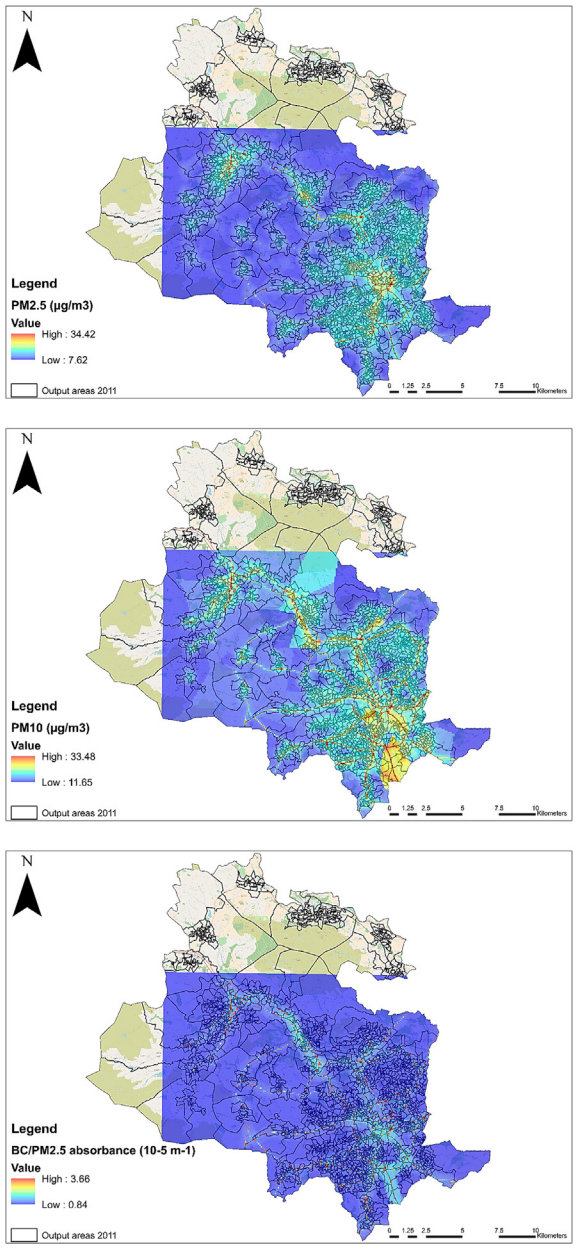

Fig. 2. $PM_{2.5}$, PM_{10} and BC Spatial Distribution across Bradford (100 m × 100 m air pollution raster surfaces).

We also found another Bradford specific publication that related to a younger age group (birth to 7 years old). Mebrahtu et al. (2015) identified asthma, based on diagnostic and prescription codes in the primary care database, for 13,734 children ages birth to 7 years old, participating in the Born in Bradford cohort (Wright et al., 2013).

Using the data reported in this paper, we calculated an asthma incidence rate of *123 per 10,000 person-years*. However, and as the authors note, this figure is likely to be conservative due to diagnosis difficulties in this younger age group (Mebrahtu et al., 2015). Bradford is indeed known to have childhood asthma rates higher than national and regional averages (Yorkshire and Humber Public Health Observatory, 2012). Hence, Mebrahtu et al. (2015) also established another incidence rate in children aged birth to 7 years old for 'wheezing disorders based on treatment' which identifies the existence of at least two drug prescriptions indicated for the treatment of asthma, a minimum of 1 week, and a maximum of 12 months apart. Based on this definition, we calculated an asthma incidence rate of *442 per 10,000 person-years*.

Both incidence rates calculated from this data were used in sensitivity analyses to explore the influence of the underlying incidence rates in the BoD assessment (Künzli, 2002). We applied these birth to 7 years old incidence rates to the whole birth

to 18 years old population, even though asthma incidence rates between these two groups can greatly differ. The rationale behind this decision was to simply demonstrate the influence of the underlying incidence rates in the BoD assessment.

2.3.4. Exposure-Response functions

Exposure-response functions for the association between exposure to air pollution and the subsequent development of childhood asthma from birth to 18 years old were extracted from random effects meta-analyses reported in Khreis et al. (2017). The meta-analyses reported in Khreis et al. (2017) synthesized studies that examined the association between children's exposure to TRAP metrics and their risk of subsequent 'asthma' incidence or lifetime prevalence, from birth to age 18 years old. Random-effects meta-analyses were selected to summarize the risk estimates across the range of studies, as they account for within study variance caused by chance and sampling error, but also for between studies variance caused by heterogeneity (Kirkwood and Sterne, 2003), a feature that is likely to be present in studies of TRAP exposures and asthma development (Health Effects Institute, 2010).

The $PM_{2.5}$ exposure-response function was based on 10 studies and equaled OR = 1.03 (95% CI, 1.01–1.05), per 1 $\mu g/m^3$ $PM_{2.5}$. The PM_{10} exposure-response function was based on 12 studies and equaled OR = 1.05 (95% CI, 1.02–1.08), per 2 $\mu g/m^3$ PM_{10}. The BC exposure-response function was based on 8 studies and equaled OR = 1.08 (95% CI, 1.03–1.14), per 0.5 $\times 10^{-5}$ m^{-1} BC.

Detailed information on the derivation of these exposure-response functions can be found in the original paper (Khreis et al., 2017). It is worth noting here that the studies included in the underlying meta-analyses *did not* adjust for co-pollutants. As such, the numbers of asthma cases attributable to $PM_{2.5}$, PM_{10} and BC should *not* be added up. Instead, these estimates should be viewed as independent estimates of the potential impact of traffic-related air pollutants on childhood asthma burden.

2.3.5. Estimation of population attributable fraction and attributable number of cases

Using the exposure-response functions above, the risk estimates for asthma development were scaled to the difference in exposure level between the counterfactual (no or zero exposure) and the reference (current exposure) scenarios. To scale a risk estimate (as estimated from the exposure-response functions) to the exposure difference between the reference and the counterfactual scenarios, standard methods were used (Mueller et al., 2017):

$$RR_{exposure\_difference} = e^{\left(\left(\frac{\ln RR}{E_{RR\_unit}}\right) \times E_{exposure\_difference}\right)}$$

where RR is the relative risk obtained from the exposure-response function; E_{RR_unit} is the exposure unit that corresponds to the RR obtained from the exposure-response function; $E_{exposure_difference}$is the difference in the exposure level between the counterfactual scenario and the reference scenario; $RR_{exposure\_difference}$ is the scaled relative risk that corresponds to the difference in exposure level between the counterfactual (no exposure) and reference (current exposure) scenario.

The PAF was then calculated, as below. The PAF defines the proportional reduction in morbidity that would occur if the exposure to air pollution was reduced to the counterfactual (no or zero exposure) scenario:

$$PAF = \frac{\sum_{i=1}^{n} P(RR_{exposure\_difference} - 1)}{\sum_{i=1}^{n} P(RR_{exposuredifference} - 1) + 1}$$

where P is the proportion of the exposed population (100% assumed); $RR_{exposure\_difference}$ is the previously scaled RR that corresponds to the difference in exposure level between the counterfactual (no exposure) and reference (current exposure) scenario; n is the number of exposure levels.

Finally, the number of childhood asthma cases attributable to the excess exposure compared to the counterfactual (no or zero exposure) scenario was calculated as follows:

$$Attributable\ number\ of\ asthmacases = PAF * expected\ asthma\ cases\ due\ to\ all\ causes$$

where: $Expected\ asthma\ cases\ due\ to\ all\ causes = childhood\ population * baseline\ childhood\ asthma\ incidence\ rate$.

2.3.6. Estimation of the impact of exposure scenarios

As described above, the counterfactual exposure reduction scenario that we used to estimate the BoD was the reduction of air pollution to zero (i.e. no exposure). This, of course, is an unrealistic scenario, the aim of which was not to assess the impact of a plausible policy *per se* but rather to estimate the overall number of asthma cases attributable to air pollution and subsequently its traffic component. Further, there is no evidence that health effects do not occur under a particular safe level of air pollution concentrations and therefore policy efforts should aim at reducing air pollution as much as possible.

As another more plausible exposure reduction scenario, air pollutants at each output area that exceeded the WHO air quality guideline values (Krzyzanowski and Cohen, 2008), were reduced to comply with the guidelines. This scenario was applicable to two of the three pollutants studied, as BC has no air quality guideline yet:

- $PM_{2.5}$ reduced to 10 $\mu g/m^3$ (annual average)
- PM_{10} reduced to 20 $\mu g/m^3$ (annual average)

The number of preventable asthma cases attributable to these scenarios was calculated. Again, these estimates are only indicative as there is no evidence that health effects do not occur under these "thresholds" (Health Effects Institute, 2010).

3. Results

3.1. Output areas $PM_{2.5}$, PM_{10} and BC exposure estimates

Fig. 2. shows the $PM_{2.5}$, PM_{10} and BC air pollution (raster) surfaces, with a resolution of 100 m × 100 m. At the output area level, the annual average exposure estimates for $PM_{2.5}$, PM_{10} and BC were 10.40 $\mu g/m^3$, 16.63 $\mu g/m^3$ and 1.07×10^{-5} m^{-1}, respectively. Table 4 shows the distribution of the $PM_{2.5}$, PM_{10} and BC average exposures across the output areas included in the analysis.

3.2. Attributable number of cases

Using the national incidence rate of childhood asthma, we estimated that an average of 488 (range = 182, 732) childhood asthma cases per year, or 27% of all childhood asthma cases in Bradford, were attributable to $PM_{2.5}$. For PM_{10}, we estimated an average of 612 (range = 279, 866) attributable asthma cases per year, or 33% of all childhood asthma cases. Finally, for BC, we estimated an average of 279 (range = 113, 447) attributable asthma cases per year, or 15% of all childhood asthma cases in Bradford (Table 5).

3.3. The impact of different baseline childhood asthma incidence rates

We investigated the impact of using differing local baseline asthma incidence rates, as calculated from Mebrahtu et al. (2015). Compared to the main analyses (Table 5), the number of the estimated attributable asthma cases drops by 11% when using the first lower asthma incidence rate (123 per 10,000 person-year) whilst it rises by 322% when using the second higher asthma incidence rate (442 per 10,000 person-year) which is based on treatment (Table 6).

Table 4
$PM_{2.5}$, PM_{10} and BC Annual Average Pollutant Concentrations across Included Output Areas.

Statistic	Minimum	1st quartile	Median	Mean	3rd quartile	Maximum
$PM_{2.5}$ ($\mu g/m^3$)	7.67	9.62	10.31	10.40	10.97	26.13
PM_{10} ($\mu g/m^3$)	12.17	15.54	16.53	16.63	17.65	27.94
$BC/PM_{2.5\ absorbance}$ (10^{-5} m^{-1})	0.85	0.90	0.99	1.07	1.16	3.60

Table 5
Estimated Annual Attributable Childhood Asthma Cases in Bradford using the $PM_{2.5}$, PM_{10} and BC LUR Models (baseline asthma incidence = 137 per 10,000 person-year, baseline asthma incident cases = 1827).

Pollutant	Attributable cases	Attributable cases lower CI	Attributable cases upper CI	Percentage of all cases
$PM_{2.5}$	488	182	732	27%
PM_{10}	612	279	866	33%
$BC/PM_{2.5\ absorbance}$	279	113	447	15%

Table 6
Estimated Annual Attributable Childhood Asthma Cases in Bradford using the $PM_{2.5}$, PM_{10} and BC LUR Models and Differing B*aseline Asthma Incidence Rates.*

Baseline asthma incidence = 123 per 10,000 person-year Baseline asthma incident cases = 1641				
Pollutant	Attributable cases	Attributable cases lower CI	Attributable cases upper CI	Percentage of all cases
$PM_{2.5}$	438	163	657	27%
PM_{10}	549	250	778	33%
$BC/PM_{2.5\ absorbance}$	250	101	402	15%
Baseline asthma incidence = 442 per 10,000 person-year Baseline asthma incident cases = 5896				
$PM_{2.5}$	1574	586	2363	27%
PM_{10}	1974	900	2794	33%
$BC/PM_{2.5\ absorbance}$	899	364	1443	15%

Table 7
Estimated Annual Attributable Childhood Asthma Cases in Bradford using the traffic-related $PM_{2.5}$, PM_{10} and BC concentrations (baseline asthma incidence = 137 per 10,000 person-year, baseline asthma incident cases = 1827).

Pollutant	Attributable cases	Attributable cases lower CI	Attributable cases upper CI	Percentage of all cases
$PM_{2.5}$	127	47	190	7%
PM_{10}	202	92	286	11%
$BC/PM_{2.5\ absorbance}$	215	87	344	12%

3.4. The impact of the exposure reduction scenario

Table 4 shows that mean pollutant concentrations estimated at the output areas' level were low overall. There were 878 output areas which exceeded the annual WHO air quality guideline of 10 $\mu g/m^3$ for $PM_{2.5}$ and 64 which exceeded the PM_{10} guideline of 20 $\mu g/m^3$. Although the number of output areas that exceeded the $PM_{2.5}$ air quality guideline was high, the exceedances were only by 1 $\mu g/m^3$, on average. Compliance with the $PM_{2.5}$ guideline prevented 29 asthma cases whilst compliance with the PM_{10} guideline prevented 2 asthma cases only.

3.5. Estimation of the contribution of traffic

As shown in Table 1, 26% of urban $PM_{2.5}$, 33% of urban PM_{10} and 77% of urban BC in Bradford are, on average, specifically due to road traffic. In a simplistic exercise, we scaled the number of childhood asthma cases attributable to overall urban $PM_{2.5}$, PM_{10} and BC concentrations (Table 5) by the traffic contribution of each pollutant. As such we estimated the number of cases specifically attributable to TRAP (air pollution specifically originating from road traffic). The results are shown in Table 7 and indicate that 7%, 11% and 12% of childhood asthma cases were specifically attributable to the traffic-related component of $PM_{2.5}$, PM_{10} and BC, respectively.

4. Discussion

4.1. Summary

This study provides one of the very few BoD assessments of TRAP and the incidence of childhood asthma; using pollutant-specific exposure estimates (rather than exposure surrogates such as residential proximity to major roadways (Perez et al., 2013)) and pollutant-specific meta-analytic exposure-response functions (rather than a single study's exposure-response function (McConnell et al., 2006)). Further, this study provides new information on the BoD estimates' variability depending on the pollutant's selection, across three commonly studied pollutants: $PM_{2.5}$, PM_{10} and $BC/PM_{2.5\ absorbance}$.

Depending on which pollutant is considered the putative agent, the results indicated that 15%–33% of new childhood asthma cases in Bradford are attributable to the exposure to air pollution, on an annual basis. In particular, 27%, 33% and 15% of all new annual childhood asthma cases in Bradford can be attributable to $PM_{2.5}$, PM_{10} and BC exposures, respectively (Tables 5 and 6). These results differ from previous estimates attributable to NO_2 and NO_x by up to 23%, in the most divergent case (childhood asthma cases attributable to BC are 23% less than those attributable to NO_x) (Khreis et al., 2018). The traffic-related component of air pollution was responsible for 7% to 12% of childhood asthma cases, with BC serving as the pollutant most specific to road traffic. The numbers of asthma cases attributable to each pollutant should *not* be added up, and instead viewed as independent estimates of the potential impact of traffic-related air pollutants on childhood asthma burden. Which is the putative agent remains an open question.

Using differing baseline asthma incidence rates also resulted in higher or lower estimates and this is an issue that is particularly important if those impacts are monetized. The exposure reduction scenario we tested had little impact on the BoD estimates but the modeling and averaging of air pollution over the output areas might conceal/attenuate the potential impacts.

4.2. Addition to the literature

This study adds to a very limited evidence base documenting the impact of intra-urban air pollution on the childhood asthma BoD. The study addresses some important limitations in past research but also highlights multiple areas that warrant further work. Both the additions to the literature and future work needed are discussed next.

Until this year (Khreis et al., 2018), published studies on childhood asthma BoD and TRAP relied on residential proximity to major roadways as the TRAP exposure metric (Perez et al., 2009; Perez et al., 2013; Künzli et al., 2008; Perez et al., 2012). Despite its arguable specificity to traffic, proximity to major roadways is a dichotomous and crude exposure metric (Brook, 2012; Khreis and Nieuwenhuijsen, 2017). It is sensitive to confounding by socio-economic factors and cannot provide information on the impacts of actual pollutants and their current, or counterfactual, concentrations in ambient air (Beevers et al., 2013; Khreis and Nieuwenhuijsen, 2017). When using proximity to major roadways as the TRAP exposure metric, subjects

residing within a certain distance from certain roads are assumed to have equal exposures (Ryan et al., 2007a). This is a flawed assumption that disregards the impacts of meteorological factors, site layout and different traffic fleet mixes on ambient air pollution and exposure levels. Indeed, previous work showed that using proximity to roadways as a TRAP exposure surrogate can result in categorizing infants as "unexposed" whilst using a LUR model with continuous exposures would result in categorizing the same infants as exposed, but to the lowest TRAP levels (Ryan et al., 2007a). The range of exposure estimates one can obtain with LUR or similar models is a more realistic exposure characterization than designated discrete exposure categories from a proximity model (i.e. exposed versus unexposed) (Ryan et al., 2007b). Further, this metric does not consider the compounded effects of proximity to multiple roads (Beevers et al., 2013; Khreis and Nieuwenhuijsen, 2017).

Second, the exposure-response function underlying all previous BoD assessmentswas sourced from an individual analysis (McConnell et al., 2006), rather than a meta-analysis. This may be argued as preferable in the Southern Californian studies (Künzli et al., 2008; Perez et al., 2009; Perez et al., 2012), where the use of a location-specific exposure-response function to calculate the same location's attributable fraction is appropriate. However, in the European-wide study, the use of an individual US study's exposure-response function for a large European population is less appropriate (Perez et al., 2013). Often and preferably in BoD assessments, exposure-response functions should be sourced from meta-analyses. Meta-analytic exposure-response functions are considered as the best available and the most generalizable evidence that can best be extrapolated to the population of interest, in the common lack of population-specific exposure-response functions (Nieuwenhuijsen et al., 2017; Mueller, 2017).

Third, uncertainties in the BoD estimates due to uncertainties in baseline asthma incidence rates have not been examined previously. This is important, especially in the context of childhood asthma, where the consensus on the condition's definition is poor (Khreis et al., 2017; van Schayck and Boudewijns, 2017).

In this study, we addressed the above issues as follows. For the exposure assessment, we used estimates from highly resolved LUR models which provided information on three different pollutants and compared these estimates to previous estimates attributable to NO_x and NO_2 (Khreis et al., 2018). Furthermore, we used newly generated exposure-response functions from meta-analyses combining information from studies specifically focused on TRAP exposures as a risk factor for childhood asthma development (Khreis et al., 2017). We explored the uncertainties in the BoD estimates due to uncertainties in the asthma incidence rates by using national versus local baseline incidence rates with differing underlying asthma definitions. We showed that the pollutant and the baseline incidence rate selection make tangible differences to the final BoD estimates, and therefore should be considered carefully in future assessments.

4.3. Future work and open questions

There are key limitations to this study and questions which remain open. First, the use of the LUR model to estimate exposures did not allow us to disentangle the contribution of the different sources to the ambient air pollution concentrations. As such, we could not attribute specific percentages of the BoD back to the responsible sources. We were however fortunate to have the ratios between traffic and urban background site concentrations for $PM_{2.5}$, PM_{10} and BC from the ESCAPE measurements. In a simplistic but indicative exercise, we used these ratios and quantified the BoD specifically attributable to TRAP. We showed that BC was the pollutant most specific to road traffic in the study area.

Whilst there is general consensus that intra-urban spatial variability in air pollution concentrations is dominated by road traffic (Favarato et al., 2014; Khreis et al., 2017), the validity of this statement depends on the pollutant studied (Wu et al., 2015; Wheeler et al., 2008). For example, NO_2, NO_x and BC are generally accepted as traffic-related air pollutants, especially heavy duty and diesel-powered traffic (Wu et al., 2015; Krämer et al., 2009; Cyrys et al., 2003). On the other hand, variations in $PM_{2.5}$ and PM_{10} are more associated with regional sources and traffic factors alone cannot capture these pollutants' variability (Wu et al., 2015; Krämer et al., 2009).

Future work should investigate the sources of air pollution and as such attribute the estimated BoD to the different sources responsible for PM and BC. This can be done using full-chain models (Khreis et al., 2018) or equivalent methods such as source apportionment. Tracing the health impacts back to the specific air pollution sources that cause them can greatly aid policy recommendation and design and guide future research.

Another limitation related to assigning the exposure estimates at the output area level. This practice is commonplace in the literature and it is extremely difficult to assess personal or residential exposures for the large populations that are usually included in BoD studies (for example, 143,472 children in this study). However, average exposures at the census tract level cannot fully capture the actual exposure variability in the population (Mueller, 2017). Exposure variability may be due to the population mobility as it is unknown whether the population studied spend most of their time in their residential census tracts or elsewhere, or due to the high variability in air pollution levels within the census tracts themselves. This is expected to result in exposure misclassification (Nieuwenhuijsen, 2015) and consequently distort the estimated BoD.

Finally, an important question that remains open is which are the putative agents in the TRAP mixture? Recent reports suggest that NO_2, although commonly studied, may not be the putative agent, but instead may act as a surrogate for traffic-related BC, toxic particles (PM), other unmeasured traffic-related air pollutants and/or the mixture (Health Effects Institute, 2016). However, many epidemiological studies lack data on and control for multiple pollutants. This makes a distinction of pollutant-specific effects not possible. Future work should expand the focus on NO_2 to other traffic-related pollutants including BC, NO_x, PM, ultra-fine particles and particle constituents. Future work would also benefit from looking at toxicological

research that may help ground epidemiological observations and identify underlying mechanisms driving the observed effects.

5. Conclusions

This study provides a BoD assessment of TRAP and the incidence of childhood asthma using meta-analytic and pollutant-specific exposure-response functions. Air pollution, and TRAP specifically, are estimated to cause a large, but largely preventable, childhood asthma burden. Between 15% and 33% of all annual childhood asthma cases in Bradford may be associated with urban air pollution, whilst 7% to 12% of all annual childhood asthma cases may be specifically associated with the traffic-related component of air pollution. Our findings underlie the need to reduce childhood exposure to air pollution and TRAP through transport and land-use policies. We show that the selection of the pollutant in the BoD assessment makes a measurable impact on the final estimates. The most suitable pollutant to be used in future BoD exercises, however, is unclear. Future work would benefit from research presenting data and results for multiple pollutants and from a better integration with toxicological findings that may shed light on the putative agent(s).

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Competing financial interests

The authors declare they have no competing interests.

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