# Near Fatal and Fatal Asthma and Air Pollution – are we missing an opportunity to ask key questions?

**Citation for published version:**
Varghese, D, Clemens, T, McMurray, A, Pinnock, H, Grigg, J & Cunningham, S 2023, 'Near Fatal and Fatal Asthma and Air Pollution – are we missing an opportunity to ask key questions?', *Archives of Disease in Childhood*. https://doi.org/10.1136/archdischild-2023-325548

**Digital Object Identifier (DOI):**
10.1136/archdischild-2023-325548



**Published In:**
Archives of Disease in Childhood

# Title: Near Fatal and Fatal Asthma and Air Pollution – are we missing an opportunity to ask key questions?

Dr Deepa Varghese[1,2], Dr Tom Clemens[3], Dr Ann McMurray[4], Professor Hilary Pinnock[2], Professor Jonathan Grigg[5], Professor Steve Cunningham[1]

1. Department of Child Life and Health, University of Edinburgh, Edinburgh, United Kingdom
2. Asthma UK Centre for Applied Research, Usher Institute, University of Edinburgh
3. University of Edinburgh, Edinburgh, United Kingdom
4. Royal Hospital for Children and Young People, Edinburgh, United Kingdom
5. Centre for Child Health, Blizard Institute, Queen Mary University of London, London, United Kingdom

Corresponding author: Dr Deepa Varghese, Department of Child Life and Health, University of Edinburgh, Royal Hospital for Children and Young People, 50 Little France Cres, Edinburgh EH16 4TJ United Kingdom; deepa.varghese@ed.ac.uk

**ABSTRACT**

There is an increasing body of evidence supporting the link between asthma attacks and air pollution in children. To our knowledge, there has only been one reported case of a fatal asthma attack in a child associated with air pollution and this was in the UK. This article considers why there is a lack of evidence on fatal asthma and air pollution. We also explore three challenges. (1) Fatal and near fatal asthma events are rare and not yet well understood. (2) Measuring and interpreting personal exposure to air pollution with sufficient temporal and spatial detail is challenging to interpret in the context of individual fatal or near fatal asthma attacks. (3) Current studies are not designed to answer the question of whether or to what extent air pollution is associated with fatal/near fatal asthma attacks in children. Conclusive evidence is not yet available and systems of data collection for both air pollution and fatal and near fatal asthma attacks should be enhanced to ensure risk can be determined and impact minimised.

## Introduction

Ella Kissi-Debrah was the first person in the United Kingdom (UK) whose death, at 9 years of age, was attributed to air pollution [1]. Residing in a busy, traffic dense area of London, Ella was exposed to high levels of traffic-related air pollution (TRAP). Her severe asthma symptoms and eventual death were attributed to exposure to high levels of outdoor air pollution. Asthma deaths in the UK are amongst the highest in Europe[2]. Whilst clinicians are aware of this statistic and measures have been suggested to reduce risk[3], strategies to reduce air pollution exposure are not at the forefront of our consultations and clinicians lack the tools and knowledge to limit exposure. If outdoor air pollution could be a significant contributing factor to near fatal and fatal asthma attacks, why are we not doing more to understand and prevent further cases?

## Air pollution

Hippocrates in 400BC wrote of air pollution concerns in *Air, waters and places* (400BC)[4]. A more contemporaneous, but archaic vision of air pollution is the London smog of December 1952 when a weather event combined with high levels of industrial air pollution caused a visible smoke cloud which was estimated to cause 4000 deaths[5]. Current harmful levels of air pollution are often not visible to the naked eye and yet silently contribute to an estimated 28 000 to 36 000 deaths per year in the UK[6].

Outdoor air pollution levels are a global health concern and are estimated to contribute to 4.2 million premature deaths globally[7]. Air pollution has a negative impact on health in utero, during childhood and in adulthood[8]. The World Health Organisation (WHO) identifies sulphur dioxide ($SO_2$), nitrogen dioxide ($NO_2$), Ozone ($O_3$) carbon monoxide (CO) and Particulate Matter (PM) as the main air pollutants negatively impacting on health outcomes. Other pollutants such as benzene have also been attributed to negative health outcomes in children with asthma[9]. The main sources of each vary (Table 1). Particulate matter (PM) is made up of solid and or liquid materials of differing size which be primary or secondary components[10] and is further quantified by size: <1 µm, ≤2.5µm and ≤10 µm. Outdoor air pollutants are typically measured from a distribution of fixed location monitoring stations. Local levels are modelled based on these measurements combined with meteorological patterns, taking into account the chemical reaction of different pollutants in the atmosphere to produce secondary pollutants[11]. In the UK, levels of air pollutants are reported in relation to the Air Quality Standards Regulations 2010 which mandate limits for certain air pollutants. UK air pollution levels are currently higher than that recommended by the World Health Organisation (WHO) (see table 2).

*Table 1 Air pollutants and sources*

| ***Pollutant*** | ***Most common source*[10,12,13]** |
|---|---|
| ***Sulphur dioxide*** | *Combustion of sulphur containing fuels e.g. coal* |
| ***Nitrogen dioxide*** | *Power generation, industrial combustion and road transport* |
| ***Ozone*** | *Created by photochemical reactions involving nitrogen oxides and volatile organic compounds* |
| ***Carbon monoxide*** | *Produced from combustion of gas, oil, coal and wood* |
| ***Particulate matter*** | *Primary components*<br>*Sea salt, black carbon, trace metals mineral components, road transport – fuel combustion and tyre/brake wear, road dust*<br>*Secondary components*<br>*Sulphate, nitrates* |
| ***Benzene*** | *Vehicle exhaust, evaporation of petrol* |

*Table 2 WHO vs UK recommended levels*[7,14,15]

| ***Air pollutant*** | ***UK recommended level*** | | ***European Union*** | | ***WHO recommended level*** | |
|---|---|---|---|---|---|---|
| ***Sulphur dioxide* μm/m$^3$** | *24-hour average* | *125* | *24-hour average* | *125* | *24-hour average* | *40* |
| ***Nitrogen dioxide* μm/m$^3$** | *Annual* | *40* | *Annual* | *40* | *Annual* | *10* |
| | *24-hour average* | *No limit set* | *24-hour average* | *No limit set* | *24-hour average* | *25* |
| ***Ozone* μm/m$^3$** | *Annual* | *No limit set* | *Annual* | *No limit set* | *Annual* | *60* |
| | *24-hour average* | *No limit set* | *24-hour average* | *No limit set* | *24-hour average* | *100* |
| | *8 hour mean* | *100* | *8 hour mean* | *120* | *8 hour mean* | *No limit set* |
| ***Carbon monoxide* μm/m$^3$** | *24-hour average* | *10* | *24-hour average* | *No limit set* | *24-hour average* | *4* |
| ***PM 2.5* μm/m$^3$** | *Annual* | *20* | *Annual* | *25* | *Annual* | *5* |
| | *24-hour average* | *No limit set* | *24-hour average* | *No limit set* | *24-hour average* | *15* |
| ***PM 10* μm/m$^3$** | *Annual* | *40* | *Annual* | *40* | *Annual* | *15* |

| | | | | | | |
|---|---|---|---|---|---|---|
| | *24-hour average* | *50* | *24-hour average* | *50* | *24-hour average* | *45* |

## Asthma and air pollution

Asthma is one of the key respiratory conditions impacted by outdoor air pollutants. It is postulated that air pollutants physically obstruct and aggravate airways at bronchiole level[16]. Small particles and oxides can trigger the inflammatory cascade, resulting in acute bronchospasm in asthmatic airways[16–18]. Children are more vulnerable to the effects of air pollution compared to adults as they spend more time outdoors, have smaller airways and inhale a larger volume per kilogram per body mass compared to an adult[19]. Globally there is increasing evidence that outdoor air pollution adversely affects children with asthma. Air pollutants, such as particulate matter, have been found in placental phagocytes suggesting small particulates can enter the circulation and damage organ development[20,21]. Exposure to air pollution in pregnancy and infancy has been associated with the subsequent development of asthma, allergic sensitization and rhinitis in childhood[22–24] . Children exposed to air pollution can have lower lung function[25], increased asthma medication use[26,27], an increase in primary care, emergency care and hospital admissions[9,28–32]. The impact of viral infections in combination with air pollution has also been studied showing an increase in viral exacerbations of asthma when combined with higher air pollution exposure[33].

## Challenges in interpreting air pollution data

There are several factors to be considered when applying large scale air pollution data to an individual and an asthma attack at a specific time point. Firstly, the monitoring and reporting of air pollution varies from country to country due to regional variations in the types of air pollutants monitored and location of fixed monitoring stations. Urban areas are likely to have more stations within a smaller geographical radius compared to rural locations. Secondly, daily weather patterns are a significant contributing factor to air pollution exposure and extreme weather events such as thunderstorms, dust and sand storms will affect levels of air pollutants such as particulate matter[34]. Thirdly, air pollution is a broad term which is likely to refer to a mixture of pollutants, of which several or all may have an effect on asthmatic airways. Components such as particulate matter could refer to particles such as sea salt which is benign, or toxic industrial gaseous waste. Studies commonly address air pollutants individually and although this is useful, air pollutants are highly spatially correlated and thus the effects should be mixed together in epidemiological analyses to fully estimate the effect on a respiratory condition such as asthma. Fourthly, annual mean levels are often reported as thresholds for air pollution (see Table 2). Concentrations can vary significantly over relatively short time-scales and therefore annual means may overlook substantial peaks and troughs in a congested area. Although air pollution modelling is improving as advanced algorithms provide better spatial and temporal detail estimates (including hourly estimates at 100x100m spatial resolution), more frequently recorded, granular data would support better research though such data are less commonly available.

## Personal exposure

Ideally, personal exposure to air pollutants should be considered when evaluating the impact of air pollution on health. In practice this is difficult to achieve. An individual's exposure to outdoor air pollutants will be less if they remain indoors when outdoor pollution levels are high. Children are more likely to be exposed based on activities of daily living as compared to adults, as children spend a higher proportion of their day outdoors.

Young children are closer to traffic-related air pollutants because of their small stature compared to adults which may increase exposure to air pollutants[35]. Without personal exposure measurement, the effect of air pollution globally, country wide or even regionally on an individual at the time of an attack can only be estimated based on modelled data. Exposure to indoor air pollutants have not been covered in this article but must also be taken into account when evaluating potential triggers of asthma attacks and risk factors for poor respiratory health[36].

Air pollution data related to fatal and near fatal asthma attacks is gathered retrospectively. Exposure to air pollutants around the time of an event is difficult to measure directly without personal exposure devices. Use of personal air pollution monitors has been studied in children with asthma[37,38] but it may be challenging in the context of asthma attacks which are unpredictable and may not occur when a participant is wearing a device. Measuring levels of air pollutants in a child's 'microenvironment' using personal monitoring devices may be useful when considering sources of daily exposures[38] but this has not yet been demonstrated in fatal or near fatal asthma attacks. Efforts to evaluate individual exposure (for example, from macrophages and presence of sputum carbon[39] demonstrate a possible mechanism to assess exposure, but again is of uncertain feasibility in relation to an acute severe attack. Activity diaries may be useful aids to guide personal exposure but linking personal exposure to an event will be highly individualised to each patient. The use of portable/personal devices such as spirometry may also help elucidate an association between exposure and health effects, whilst reducing exposure misclassification. Even the most robust observational study will struggle to estimate the actual exposure to air pollution around the time of an attack.

## Near fatal and fatal asthma impacted by air pollution - are there more cases to come or have we missed many in the past?

Fatal and near fatal asthma attacks cause concern and anxiety for paediatric clinicians, parents, children and young people. Fatal and near fatal asthma is rare but the UK has one of the highest death rates from asthma in age 10 – 24 years[40]. Asthma attacks in children accounted for >19 000 admissions in England and Wales in 2022[41]. Despite heightened awareness of the importance of diagnosing and appropriately managing asthma, the National Review of Asthma Deaths report concluded that care was inadequate in 13 of the 28 deaths in children and young people that they investigated. People experiencing a near fatal attack are at high risk of future severe attacks and it is important for clinicians caring for children with asthma to evaluate the risk factors and features associated with near fatal and fatal attacks with an aim to reducing future risk.

Near fatal attacks are difficult to identify in the literature. The definition of near fatal asthma (and terminology used) overlaps with severe, life threatening and status asthmaticus and the use of 'diagnostic codes' to identify 'asthma' cases in routinely collected data does not further differentiate the severity of attacks within hospital. Near fatal events can be defined (see Box 1) but studies using routine data from hospital records to identify asthma attacks, typically use 'asthma' alone to find cases. Whilst this may correctly identify a case of asthma, it does not necessarily record the severity of presentation or any subsequent hospital deterioration. If a child had a sudden collapse due to asthma and required resuscitation, this would still be coded as asthma and in the same category as a child brought in to the emergency department who was discharged on the same day. This contributes to the loss of granularity of data on near fatal and fatal events, where such attacks may exist but often poorly coded and consequently identifiable within routine data. Although large studies have demonstrated an increased frequency of acute asthma presentations associated with air pollution exposure[32], attack severity is not reported. We have only identified one study meeting the definition in Box 1 which has examined the effect of ozone and PM2.5 on near fatal asthma in children [42], which demonstrated an increase in admissions to intensive care. Two other studies included air pollution levels when assessing social deprivation and near fatal asthma, but neither focussed on this as a primary or secondary outcome[43,44]. There thus is a small body of literature examining asthma mortality and air pollution and there remains a significant and important gap in the literature regarding the impact of air pollution exposure on near fatal and fatal asthma attacks in CYP.

There are factors such as social deprivation which confound both severe asthma and air pollution. Higher concentrations of $NO_2$, PM10 and $SO_2$ are observed in areas of social deprivation in England, Scotland and Northern Ireland[45] and children from areas of higher deprivation are also more likely to be admitted to intensive care for asthma [46]. The degree of association between social deprivation, asthma and air pollution requires further observation but should be highlighted. In the UK, there is a current surveillance study examining near fatal asthma which will examine social deprivation and air pollution data around the time of event[47].

| International E-Delphi defined Near Fatal Asthma Definition[48] |
|---|

A near fatal asthma attack occurs in a person who is

- Exhausted, with severe dyspnoea, unable to speak with a silent chest.
- Respiratory arrest is considered imminent and invasive ventilation will likely be required.
- They will be responding poorly to emergency asthma therapies. This is associated with hypoxaemia, hypercarbia and a falling pH.

*Box 1*

## Conclusion

We have an opportunity now to build on past work on near fatal and fatal events and air pollution. By including air pollution in the asthma risk factors assessed in a clinical history, we can start to shape the body of evidence on fatal and near fatal attacks. By increasing awareness of air pollution in conversations with our patients or their parents in the same way we would discuss smoking, atopy, pets etc. we start to highlight air pollution as a risk factor. Whilst the policy changes on air pollution exposure at local and regional levels are controlled by politicians, as clinicians we must now start to engage and consider the potential impact of air pollution for our individual patients. The question of how much exposure to air pollution is dangerous cannot yet be answered accurately, but we can start to ask the right questions (See Box 2) Some initiatives are already in place looking at ‘clean air walks to school’ but we need to encourage our patients that these can make a difference.

The body of evidence is growing, but better data will be required to support policy makers to deliver safer, lower exposure to air pollution levels in CYP with asthma. Reducing PM 2.5 by 1micro/hour could prevent 9300 new cases of asthma/year[49] and it is predicted if the UK becomes net zero we could reduce >20 000 cases of childhood asthma[50]. The death of Ella Kissi-Debrah has highlighted the devastating influence of outdoor air pollution and the urgent need for further research to understand the impact that air pollution may have on near fatal and fatal asthma in children. By keeping air pollution in mind in our clinical practice we can raise awareness, add to the evidence and find out more about near fatal and fatal asthma cases associated with air pollution.

| Suggested questions for clinicians reviewing children experiencing asthma exacerbations |
|---|
| • How do you get to school? Do you walk beside a busy road? Do you travel to school by car?<br>• Do you need your inhaler when you are walking beside a busy the road?<br>• Do you play outside close to a busy road at break time?<br>• Do you know about clean air walks to school?<br>• Is your patient's home positioned beside a source of traffic related air pollution such as a busy road and if so, how do they ventilate their home i.e. windows open or closed during peak traffic times? |

*Box 2*

## Suggestions

1. Help to identify the severity of asthma attacks in routine data. We need to know more about fatal and near fatal attacks in children. Consider a coded definition for

near fatal asthma (See Box 1) to increase the granularity of future data on near fatal asthma.

2. Add air pollution questions to your asthma history (see Box 2) - think when are they exposed (day time activities, how long and how often)
3. Consider reporting any cases of e-Delphi defined near fatal asthma to the British Paediatric Surveillance Unit study (October 2022 to April 2024).

## Contribution Statement

All authors contributed to the research, analysis of the results and to the writing of the manuscript. All authors reviewed and revised interim drafts of the article and approved the final version. Co Authors: Dr Tom Clemens (TC), Dr Ann McMurray (AM), Professor Hilary Pinnock (HP), Professor Jonathan Grigg (JG) and Professor Steve Cunningham (SC).


## Funding Statement

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.


## Competing interests

There are no competing interests for any author.

## References


1 Dyer C. Air pollution from road traffic contributed to girl’s death from asthma, coroner concludes. *BMJ*. 2020;371:m4902. DOI: https://doi.org/10.1136/bmj.m4902

2 Lung conditions kill more people in the UK than anywhere in Western Europe | Asthma + Lung UK. https://www.asthmaandlung.org.uk/media/press-releases/lung-conditions-kill-more-people-uk-anywhere-western-europe (accessed 11 May 2023)

3 Why asthma still kills. RCP London. 2015. https://www.rcplondon.ac.uk/projects/outputs/why-asthma-still-kills (accessed 11 May 2023)

4 Fowler D, Brimblecombe P, Burrows J, *et al.* A chronology of global air quality. *Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences*. 2020;378:20190314. DOI: https://doi.org/10.1098/rsta.2019.0314

5 The Great Smog of 1952. Met Office. https://www.metoffice.gov.uk/weather/learn-about/weather/case-studies/great-smog (accessed 11 May 2023)

6 Air pollution: applying All Our Health. GOV.UK. https://www.gov.uk/government/publications/air-pollution-applying-all-our-health/air-pollution-applying-all-our-health (accessed 28 September 2023)

7 Ambient (outdoor) air pollution. https://www.who.int/news-room/fact-sheets/detail/ambient-(outdoor)-air-quality-and-health (accessed 28 April 2022)

8 Every breath we take: the lifelong impact of air pollution. RCP London. 2016. https://www.rcplondon.ac.uk/projects/outputs/every-breath-we-take-lifelong-impact-air-pollution (accessed 20 January 2022)

9 Thompson AJ, Shields MD, Patterson CC. Acute Asthma Exacerbations and Air Pollutants in Children Living in Belfast, Northern Ireland. *Archives of Environmental Health: An International Journal*. 2001;56:234–41. DOI: 10.1080/00039890109604447

10 Department for Environment, Food and Rural Affairs. Air Quality Expert Group. Particulate matter in the United Kingdom.[Internet] 2005 (Accessed 28 Sept 2023). Available from: https://uk-air.defra.gov.uk/library/assets/documents/reports/aqeg/Particulate_Matter_in_The_UK_2005_Summary.pdf

11 San José R, Baklanov A, Sokhi RS, *et al.* Air Quality Modeling. In: Jørgensen SE, Fath BD, eds. *Encyclopedia of Ecology*. Oxford: Academic Press 2008:111–23. DOI:10.1016/B978-008045405-4.00201-9

12 Department of Health and Social Care. Chief Medical Officer's Annual Report [Internet] 2022.(Accessed 28 Sept 2023) Available from: https://www.gov.uk/government/publications/chief-medical-officers-annual-report-2022-air-pollution

13 Benzene: general information. GOV.UK. https://www.gov.uk/government/publications/benzene-general-information-incident-management-and-toxicology/benzene-general-information (accessed 11 May 2023)

14 Department for Environment, Food and Rural Affairs. Air Quality Objectives Update.[Internet] 2010 (Accessed 28 Sept 2023) Available from: https://uk-air.defra.gov.uk/air-pollution/uk-limits

15 Official Journal of the European Union. European Parliament resolution of 25 March 2021 on the implementation of the Ambient Air Quality Directives: Directive 2004/107/EC and Directive 2008/50/EC (2020/2091(INI)) [Internet] (Accessed 28 Sept 2023) Available from https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A52021IP0107

16 Guarnieri M, Balmes JR. Outdoor air pollution and asthma. *Lancet*. 2014;383:1581–92. DOI: 10.1016/S0140-6736(14)60617-6

17 Esposito S, Tenconi R, Lelii M, *et al.* Possible molecular mechanisms linking air pollution and asthma in children. *BMC Pulmonary Medicine*. 2014;14:31. DOI: https://doi.org/10.1186/1471-2466-14-31

18 Glencross DA, Ho T-R, Camiña N, *et al.* Air pollution and its effects on the immune system. *Free Radical Biology and Medicine*. 2020;151:56–68. DOI: 10.1016/j.freeradbiomed.2020.01.179

19 Bateson TF, Schwartz J. Children's Response to Air Pollutants. *Journal of Toxicology and Environmental Health, Part A*. 2007;71:238–43. DOI: 10.1080/15287390701598234

20 Liu NM, Miyashita L, Maher BA, *et al.* Evidence for the presence of air pollution nanoparticles in placental tissue cells. *Science of The Total Environment*. 2021;751:142235. DOI: 10.1016/j.scitotenv.2020.142235

21 Whitehouse A, Grigg J. Air pollution and children's health: where next? *BMJ Paediatrics Open*. 2021;5:e000706.DOI http://dx.doi.org/10.1136/bmjpo-2020-000706

22 Pedersen C-ET, Eliasen AU, Ketzel M, *et al.* Prenatal exposure to ambient air pollution is associated with early life immune perturbations. *Journal of Allergy and Clinical Immunology*. 2023;151:212–21. DOI: 10.1016/j.jaci.2022.08.020

23 Sbihi H, Tamburic L, Koehoorn M, *et al.* Perinatal air pollution exposure and development of asthma from birth to age 10 years. *European Respiratory Journal*. 2016;47:1062–71. DOI: 10.1183/13993003.00746-2015

24 Dick S, Doust E, Cowie H, *et al.* Associations between environmental exposures and asthma control and exacerbations in young children: a systematic review. *BMJ OPEN*. 2014;4:003827. DOI: 10.1136/bmjopen-2013-003827

25 Gauderman WJ, Urman R, Avol E, *et al.* Association of Improved Air Quality with Lung Development in Children. *New England Journal of Medicine*. 2015;372:905–13. DOI: 10.1056/NEJMoa1414123

26 Gent J, Koutrakis P, Belanger K, *et al.* Symptoms and Medication Use in Children with Asthma and Traffic-Related Sources of Fine Particle Pollution. *ENVIRONMENTAL HEALTH PERSPECTIVES*. 2009;117:1168–74. DOI: 10.1289/ehp.0800335

27 Casas L, Simons K, Nawrot T, *et al.* Respiratory medication medication sales and urban air pollution in Brussels (2005 to 2011). *ENVIRONMENT INTERNATIONAL*. 2016;94:576–82. DOI: 10.1016/j.envint.2016.06.019

28 Sinclair A, Melly S, Tolsma D, *et al.* Childhood asthma acute primary care visits, traffic, and traffic-related pollutants. *JOURNAL OF THE AIR & WASTE MANAGEMENT ASSOCIATION*. 2014;64:561–7. DOI: 10.1080/10962247.2013.873093

29 Lee J-T, Cho Y-S, Son J-Y. Relationship between ambient ozone concentrations and daily hospital admissions for childhood asthma/atopic dermatitis in two cities of Korea during 2004-2005. *Int J Environ Health Res*. 2010;20:1–11. DOI: 10.1080/0960312090325403330 Lee SL, Wong WHS, Lau YL. Association between air pollution and asthma admission among children in Hong Kong. *Clinical and Experimental Allergy*. 2006;36:1138–46. DOI: 10.1111/j.1365-2222.2006.02555.x

31 Perez L, Declercq C, Inĩguez C, *et al.* Chronic burden of near-roadway traffic pollution in 10 European cities (APHEKOM network). *European Respiratory Journal*. 2013;42:594–605. DOI: 10.1183/09031936.00031112

32 Orellano P, Quaranta N, Reynoso J, *et al.* Effect of outdoor air pollution on asthma exacerbations in children and adults: Systematic review and multilevel meta-analysis. *PLOS ONE*. 2017;12:e0174050. DOI: 10.1371/journal.pone.0174050

33 Altman MC, Kattan M, O'Connor GT, *et al.* Associations between outdoor air pollutants and non-viral asthma exacerbations and airway inflammatory responses in children and adolescents living in urban areas in the USA: a retrospective secondary analysis. *The Lancet Planetary Health*. 2023;7:e33–44. DOI: 10.1016/S2542-5196(22)00302-3

34 Darvall J.N., Durie M., Pilcher D., *et al.* Intensive care implications of epidemic thunderstorm asthma. *Crit Care Resusc*. 2018;20:294–303. PMID: 30482137.

35 Kenagy HS, Lin C, Wu H, *et al.* Greater nitrogen dioxide concentrations at child versus adult breathing heights close to urban main road kerbside. *Air Qual Atmos Health*. 2016;9:589–95. DOI: 10.1007/s11869-015-0370-3

36 Holden KA, Lee AR, Hawcutt DB, *et al.* The impact of poor housing and indoor air quality on respiratory health in children. *Breathe*. 2023;19. 230058. DOI: 10.1183/20734735.0058-2023

37 Koh L, Grigg J, Whitehouse A. Personal monitoring to reduce exposure to black carbon in children with asthma; a pilot study. *ERJ Open Research*. 2021;7:00482–2021. DOI: 10.1183/23120541.00482-2021

38 Rabinovitch N, Adams CD, Strand M, *et al.* Within-microenvironment exposure to particulate matter and health effects in children with asthma: a pilot study utilizing real-time personal monitoring with GPS interface. *Environ Health*. 2016;15:96. DOI:https://doi.org/10.1186/s12940-016-0181-5

39 Kulkarni N, Pierse N, Rushton L, *et al.* Carbon in Airway Macrophages and Lung Function in Children. *N Engl J Med*. 2006;355:21–30. DOI: 10.1056/NEJMoa052972

40 Asthma – RCPCH – State of Child Health. https://stateofchildhealth.rcpch.ac.uk/evidence/long-term-conditions/asthma/#ref-2 (accessed 20 January 2023)

41 The number of children ending up in hospital with life-threatening asthma attacks has more than doubled in the last year | Asthma + Lung UK. https://www.asthmaandlung.org.uk/media/press-releases/number-children-ending-hospital-life-threatening-asthma-attacks-has-more (accessed 11 May 2023)

42 Silverman R, Stevenson L, Hastings H. Age-related seasonal patterns of emergency department visits for acute asthma in an urban environment. *ANNALS OF EMERGENCY MEDICINE*. 2003;42:577–86. DOI: 10.1067/s0196-0644(03)00410-4

43 McDowell KM, Kercsmar CM, Huang B, *et al.* Medical and Social Determinants of Health Associated with Intensive Care Admission for Asthma in Children. *Annals ATS*. 2016;13:1081–8. PMID: 27144510

44 Grunwell JR, Opolka C, Mason C, *et al.* Geospatial Analysis of Social Determinants of Health Identifies Neighborhood Hot Spots Associated With Pediatric Intensive Care Use for Life-Threatening Asthma. *The Journal of Allergy and Clinical Immunology: In Practice*. 2022;10:981-991.e1. DOI: 10.1016/j.jaip.2021.10.065

45 Department of Environment, Food and Rural Affairs. Air Quality and Social Deprivation in the UK: an environmental inequalities analysis [Internet] 2006 (accessed 28 Sept 2023) Available from: https://uk-air.defra.gov.uk/library/reports?report_id=424

46 Mukherjee M, Cunningham S, Bhuia MR, *et al.* Asthma in paediatric intensive care in England residents: observational study. *Sci Rep*. 2022;12:1315. DOI:https://doi.org/10.1038/s41598-022-05414-5

47 BPSU Study - Near Fatal Asthma. RCPCH. https://www.rcpch.ac.uk/work-we-do/bpsu/bpsu-study-near-fatal-asthma (accessed 26 June 2023)

48 Mcmurray A, Cunningham S, Fleming L. Defining Near Fatal asthma – an international eDelphi study. Abstract for ERS Congress 2019. *European Respiratory Journal*. 2019;54. DOI:10.1183/13993003.congress-2019.PA949

49 Health matters: air pollution. GOV.UK. https://www.gov.uk/government/publications/health-matters-air-pollution/health-matters-air-pollution (accessed 11 May 2023)

50 Milner J, Hughes R, Chowdhury S, *et al.* 929 Child health benefits from reduced air pollution in 16 cities through 'net zero' greenhouse gas emissions. *Archives of Disease in Childhood*. 2022;107:A314–5. DOI: 10.1016/j.envint.2023.107972