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Diesel, children and respiratory disease

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ABSTRACT
Air pollution generated in urban areas is a global public health burden since half of the world's population live in either cities, megacities or periurban areas. Its direct effects include initiating and exacerbating disease, with indirect effects on health mediated via climate change putting the basic needs of water, air and food at risk.

INTRODUCTION
There is strong epidemiological evidence that air pollution is associated with a wide range of adverse health effects on the respiratory, cardiovascular and neurological systems.[1–3] Indeed, in the UK, the combination of new-onset (incident) diseases associated with long-term exposure, and exacerbation of diseases once disease is established results in approximately 40 000 excess deaths a year that are attributable to air pollution, increasing health service and social costs by over £20 billion a year.[2] Although deaths associated with air pollution are mainly in adults, there is also increasing concern that air pollution, especially from diesel vehicles, has major adverse effects in children and that this has long-term consequences.[4–6] In this review, we report the evidence that underpins the need for exposure reduction policy to focus on diesel vehicles and the potential beneficial effects of such a policy on children's health. Although this review focuses on the heavily dieselised UK environment, it is also relevant to countries where diesel vehicles remain a major source of emissions.

COMPONENTS OF AIR POLLUTION
The major outdoor pollutants in urban areas are inhalable particulate matter (PM, measured as either PM less than 10 µm in aerodynamic diameter (PM_{10}) or the even smaller $PM_{2.5}$), nitrogen oxides (NO_X, such as nitrogen dioxide, NO_2), ozone (O_3), sulfur dioxide (SO_2), carbon monoxide (CO) and hydrocarbons (HC). Sources of these include gasoline-powered and diesel-powered engines from vehicles, trains and, in port towns, ships (proximately PM, NO_X), vehicle tyre and brake wear (PM), power stations and factories from coal combustion and biomass burning (PM,

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What is already known on this topic?
- ► Air pollution is a global problem with negative health effects on the respiratory, cardiovascular and neurological systems.
- ► There is robust evidence that the effects of air pollution span over the life course, with growing children being particularly vulnerable.
- ► Diesel vehicles produce disproportionally more air pollution and should be a focus of exposure-mitigation policies.

What this study hopes to add?
- ► The role of emissions from diesel in contributing to exposure of UK children is reviewed.
- ► The adverse health effects of diesel emissions on UK children is reviewed.
- ► Ways of reducing exposure of children to fossil-fuel-derived air pollution in the UK, on personal and national levels, are discussed.

NO_X and SO_2),[7–9] and wood burning heating that is increasingly popular, contributing up to 9% of PM in London during winter.[10] For diesel engines, an important component of emissions is black carbon, that is, the fraction of PM that most strongly absorbs light—a component that is often called 'diesel soot'. Another pollutant, ozone, is formed by the reaction of NO_X with carbon compounds called volatile organic compounds (VOCs) in the presence of sunlight. Two of the most important VOCs emitted by vehicles are benzene and 1,3-butadiene. For emissions from diesel, there is a strong correlation between locally emitted PM_{10} and NO_X,[11] and it is reasonable to assume that, where diesel vehicles predominate, either metric is a good marker of exposure to the locally generated pollutant mix in urban areas.

WHY FOCUS ON DIESEL?
Many parts of the UK breach the EU legal limits and WHO guidelines (table 1) for pollutants on a regular basis.[12] While London often exhibits the biggest breach of pollution limits, other parts of the UK are also affected. Indeed, a recent report from the Department

Table 1 EU limits, WHO guidelines and main sources of ambient (outdoor) air pollutants. Adapted from European Commission Air Quality Standards (updated September 2017), WHO Ambient (outdoor) air quality and health fact sheet (updated Sept 2016), and Lethal and Illegal, Solving London's Air Pollution Crisis by Institute for Public Policy Research, November 2016

Pollutants	EU legal limits (averaging period)	WHO guidelines (averaging period)	Main sources
Nitrogen dioxide (NO_2)	200 µg/m³ (1 hour) 40 µg/m³ (1 year)	200 µg/m³ (1 hour) 40 µg/m³ (1 year)	Transport, combustion
Ozone (O_3)	120 µg/m³ (8 hours)	100 µg/m³ (8 hours)	Reaction of hydrocarbons, nitrogen oxides and volatile organic compounds in sunlight
Particulate matter (PM_{10})	50 µg/m³ (24 hours) 40 µg/m³ (1 year)	50 µg/m³ (24 hours) 20 µg/m³ (1 year)	Transport (exhaust, tyre, brake wear), combustion, industrial processes and construction
Particulate matter ($PM_{2.5}$)	25 µg/m³ (1 year)	10 µg/m³ (24 hours) 25 µg/m³ (1 year)	
Sulfur dioxide (SO_2)	350 µg/m³ (1 hour) 125 µg/m³ (24 hours)	500 µg/m³ (10 min) 20 µg/m³ (24 hours)	Coal combustion and road transport

of Environment Food and Rural Affairs and the Department of Transport showed 37 out of 43 reporting zones across the UK had maximum annual mean NO_2 concentrations over the EU legal limit.[13]

While there are other sources of outdoor air pollution, the largest contributor to air pollution in urban areas in the UK is road traffic, which has been rising over the last 60 years. By contrast, active forms of transport such as walking and cycling have been on a decline.[2] In the UK, approximately 50% of NO_2 emissions come from the roads,[14] with diesel engines powering half the cars and the majority of heavy vehicles.[15] At a global level, diesel vehicles contribute about 20% of NO_x.[16] As discussed above, fossil-fuel-powered engines emit carbon monoxide (CO), hydrocarbons (HC), PM and NO_x, all of which are associated with negative health effects.[17] The reason why diesel engines should be a major target for exposure-reduction strategies is that they emit more PM and NO_x than their petrol or hybrid counterparts, contributing to about 40% of all NO_x emissions in inner cities.[18 19] Furthermore, diesel, and not petrol, soot is categorised by WHO as carcinogenic[20]—a categorisation that implies that diesel PM is, mass for mass, more toxic than petrol PM. Vehicle emissions are regulated by the European Union (EU) Euro standards, currently at Euro 6 (table 2).

Table 2 EU Euro emissions standards. Adapted from Lethal and Illegal, Solving London's Air Pollution Crisis by Institute for Public Policy Research, September 2016, and SMMT Euro Standards for Cars (accessed March 2018)

Euro emissions standards	Petrol cars		Diesel cars	
	NO_x (g/km)	PM_{10} (g/km)	NO_x (g/km)	PM_{10} (g/km)
Euro 4 (2005)	0.08	–	0.25	0.025
Euro 5 (2009)	0.06	0.005	0.18	0.005
Euro 6 (2014)	0.06	0.005	0.08	0.0045

Compliance with Euro standards is assessed under laboratory conditions only and are less strict for diesel engines. But even given this leeway, recent measurements under real-life driving conditions have shown that diesel cars produce significantly more toxic emissions than the Euro standard, whereas petrol engines map closely to the laboratory Euro standard (figure 1); this phenomenon is observed globally, and Anenberg *et al*[16] reported approximately a third of heavy-duty and over half of light-duty diesel vehicle emissions breaching the certification limits, across 11 major vehicle markets. Thus, over 2000 education or childcare providers in England and Wales are located close to busy roads with concentrations of NO_x that are regularly higher than legal limits (40 µg/m³ annual mean or 200 µg/m³ 1 hour mean).[14 21 22] In addition, children attending these schools are exposed to high concentrations of freshly generated diesel pollutants during the commute to and from school and during outdoor activities (figure 2).

HEALTH EFFECTS OF DIESEL EMISSIONS ON CHILDREN
Few epidemiological studies address the effects of diesel emissions alone. However, it is reasonable to extrapolate from studies that have assessed exposure to either PM or NO_x since (1) diesel PM is not less toxic than other types of PM, and (2) the adverse effects of gases such as NO_x are independent of source. One way of estimating the health burden from diesel emissions alone is to use source apportionment data. For example, in London where most taxis, buses, heavy goods vehicles and vans are powered by diesel (table 3), 48% of NO_x and 54% of PM_{10} is from road transport (figures 3 and 4).[19 23] These vehicles, along with diesel cars, are responsible for 34% of total PM_{10} and 38% of total NO_x emissions (figures 3 and 4).[23]

Antenatal exposure
When considering effects measured in later childhood, it is difficult to separate the effect of maternal exposure
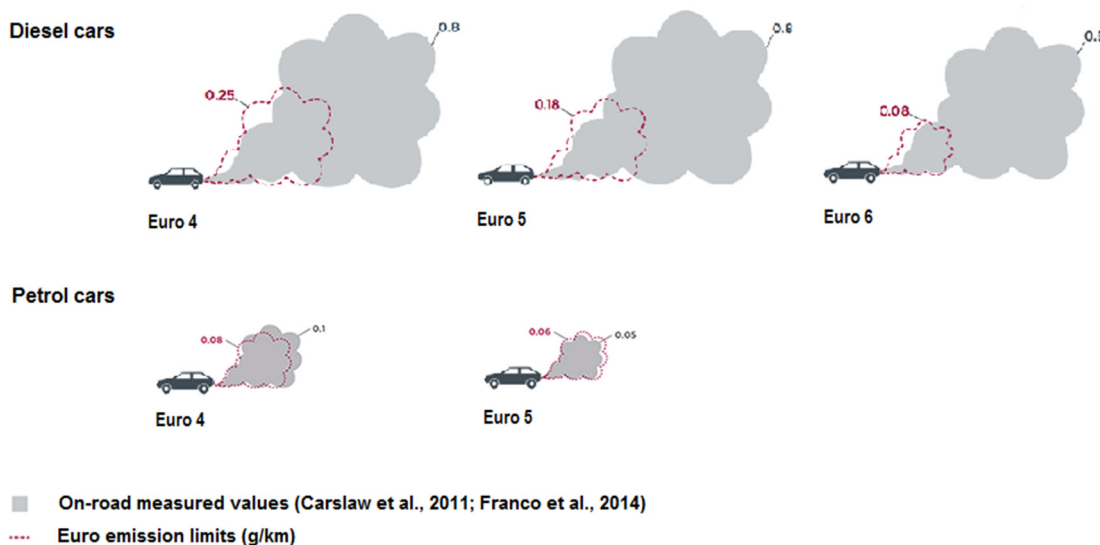
Figure 1 Real-life NO$_x$ emissions from diesel and petrol cars compared with Euro emissions standards. Adapted from the Impact of improved regulation of real-world NO$_x$ emissions from diesel passenger cars in the EU, 2015–2030 by the International Council on Clean Transportation, 2016.

to air pollution from postnatal effects—since there is a strong correlation between exposure to traffic-derived air pollutants (TRAPs) of pregnant women and their children. But independent associations between antenatal exposure to NO$_2$ and reduced FEV$_1$ later in childhood are reported. For example, Morales et al[24] reported that

an IQR increase in NO$_2$ exposure during the second trimester was associated with an estimated change in childhood FEV$_1$ by −28 mL, while the relative risk of having FEV$_1$ <80% predicted was 1.30. By contrast, effects on the fetus or on the newborn infant must be due to maternal exposure. These epidemiological studies report
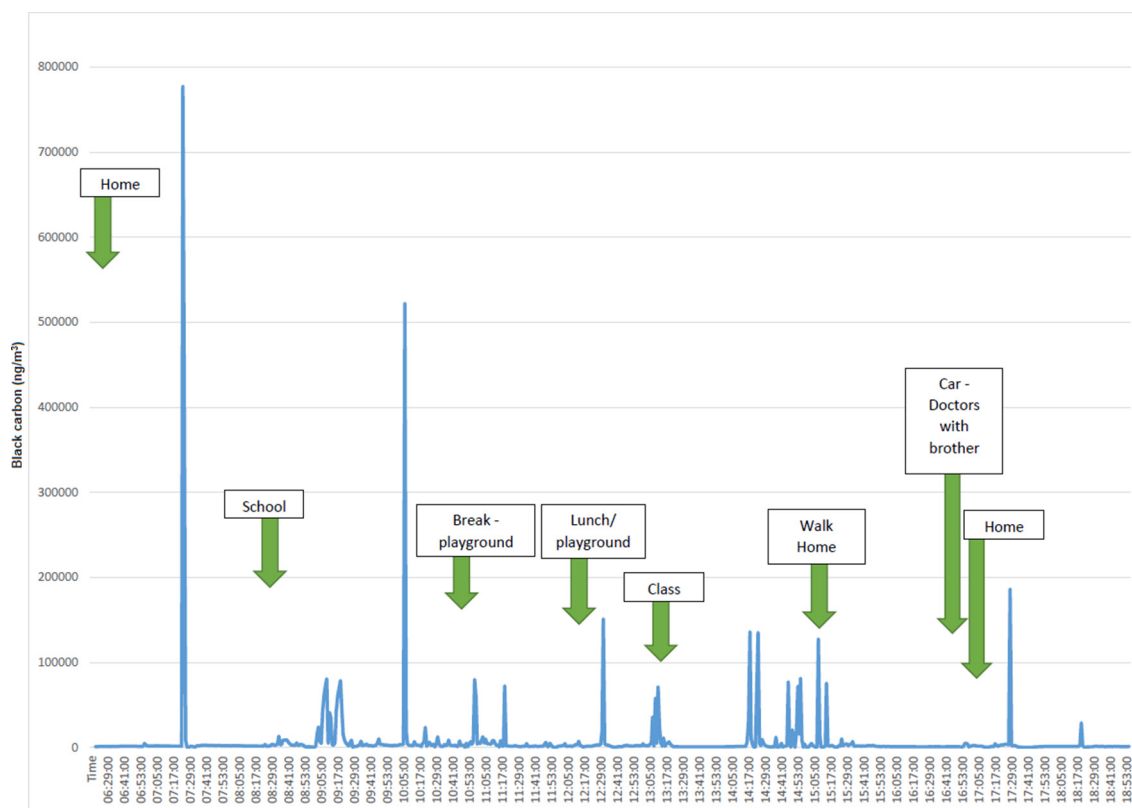

Figure 2 Black carbon levels (ng/m^3) from an aethalometer carried by a child in London on a typical school day. In London, diesel vehicles emit a disproportional amount of black carbon.

Table 3 Fuel sources of vehicles in London, 2015 (adapted from Lethal and Illegal, Solving London's Air Pollution Crisis by Institute for Public Policy Research, September 2016)

Vehicles	Petrol (%)	Diesel (%)	Other (%)
Buses	0	89	11
Taxis	0	100	0
Private vehicles	42	57	1
Light goods vehicles	2	97	1
Heavy goods vehicles	0	100	0

that maternal exposure to TRAP has adverse effects on the fetus leading to increased infant mortality, reduced fetal growth, low birth weight at term and premature birth.[25 26] Indeed, increased risk for the low birth weight for term metric is found at maternal $PM_{2.5}$ exposure lower than the EU recommended annual limit of 25 μg/m^3.[26 27] It is likely that these antenatal effects synergise with postnatal pollution exposures to increase susceptibility to common respiratory conditions such as wheeze, bronchiolitis and asthma.[28–30]

Childhood exposure

Air pollutants, particularly NO_X (reflecting exposure to both NO_X and PM), are associated with reduced lung function in children—for both FVC and FEV_1.[5] Urman et al[5] showed that an increase of 17.9 ppb of NO_X exposure was associated with a 1.56% deficit in FVC and 1.1% deficit in FEV_1, and similar findings were seen in children with or without asthma. Residing in areas with high concentrations of PM and NO_2 can also lead to suppression of

lung function growth in school children.[4 31] This reduction can potentially be halted and reversed with better air quality. For example, Gauderman et al[32] showed that reducing the levels of NO_2, PM_{10} and $PM_{2.5}$ were associated with improvements in FEV_1 and FVC growth in adolescents over 4 years—mean 4-year growth in FEV_1 increased by 91.4 mL per 14.1 ppb of NO_2 reduction, and 65.5 mL per 8.7 μg/m^3 of PM_{10} reduction, and 65.5 mL per 12.6 μg/m^3 of $PM_{2.5}$ reduction, with comparable findings in FVC. Children with existing chronic illnesses, particularly respiratory conditions, are most vulnerable. Air pollution can predispose individuals to new-onset asthma; preschool children are more prone to new onset of wheeze. A meta-analysis concluded that exposure to NO_2 is linked to new-onset asthma, while exposure to PM is linked to new-onset wheeze.[33] An effect of diesel PM per se on reactivity to inhaled allergens is supported by the association between long-term traffic pollution exposure and allergies.[34–36] Asthma exacerbations are also closely associated with short-term variations in $PM_{2.5}$.[37] Although increasing inhaled corticosteroids prior to high pollution days may seem logical,[38] it is unclear whether this strategy is effective.

There is emerging evidence that air pollution impacts on children's neurological system and development. For example, associations between exposure to air pollutants and reduced IQ and neurocognitive ability such as working memory, autism and reduced brain-derived neurotrophic factor are widely reported.[39–41] In particular, Basagaña et al[39] reported that traffic-related $PM_{2.5}$ was more strongly associated with reduction in cognitive function compared with fine particulates from other
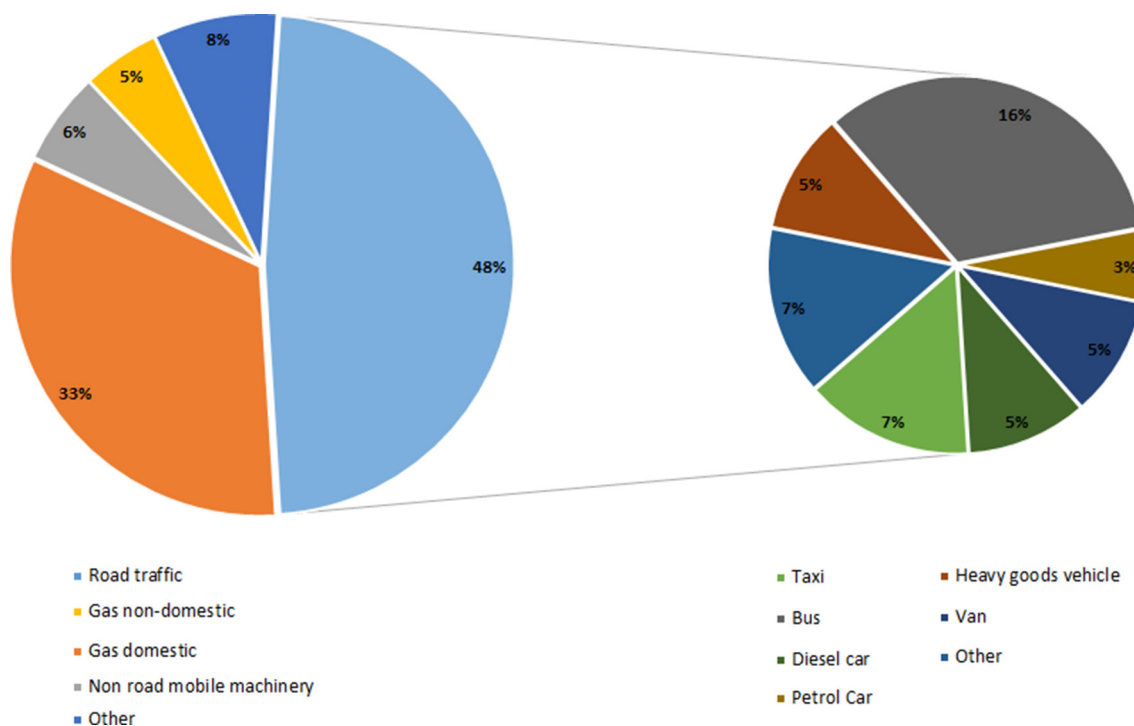

Figure 3 Sources of NO_X emissions in London, 2010. Adapted from Lethal and Illegal, Solving London's Air Pollution Crisis by Institute for Public Policy Research, November 2016.
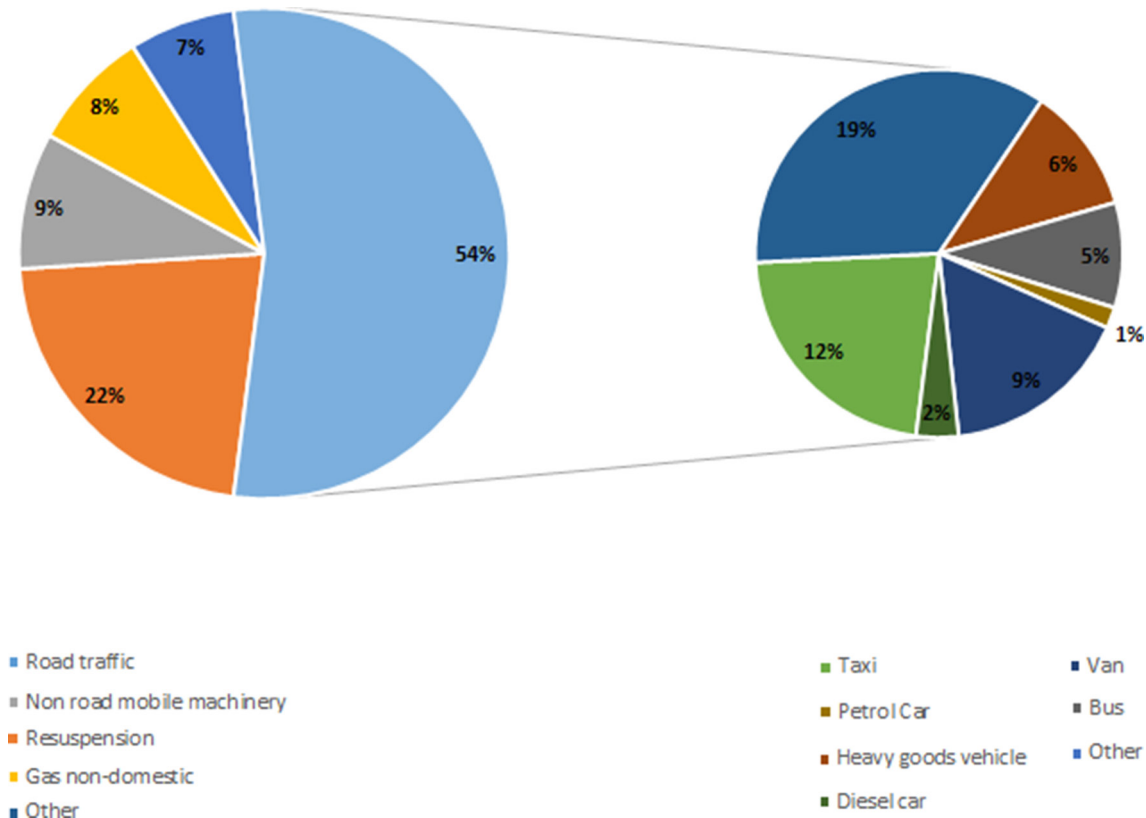
Figure 4 Sources of PM$_{10}$ emissions in London, 2010. Adapted from Lethal and Illegal, Solving London's Air Pollution Crisis by Institute for Public Policy Research, November 2016.

sources such as mineral, heavy oil combustion or road dust. In addition, exposure to high levels of traffic-induced pollutants may delay maturation of the brain.[42] An additional emerging link is between air pollution and the endocrine system. For example, Thiering *et al*[43] reported an association between insulin resistance and either NO$_2$ or PM exposure in healthy children.

Implications for adult life

It is increasingly recognised that impaired fetal well-being is a substrate for adult-onset cardiovascular disease such as atherosclerosis.[44] Prolonged exposure to air pollutants may increase mean pulmonary arterial pressure and diastolic blood pressure,[45 46] predisposing to cardiovascular events and premature death in adulthood. The effect on cognition lingers onto adulthood, where associations with dementia and Parkinson's disease have been found.[47 48]

Although the epidemiological evidence for the health effect of fossil-fuel-derived pollution is very strong, there are important confounders that must be considered. For example, in England, increased exposure to mean annual NO$_2$ concentrations is higher in areas of increased social deprivation and reduced access to healthcare.[49] Furthermore, children from more deprived areas are also more likely to be exposed to other sources of pollution such as second-hand cigarette smoking.[50]

Mechanisms

Many of the mechanisms underlying the robust epidemiological associations between air pollution and health across the life course remain to be defined. Effects on organs distant from the lung are likely to be facilitated by mediators released in the airway subsequently leaching out into the systemic circulation.[51] A key cell for release of mediators is alveolar macrophage (AM) since phagocytosis of PM by AM stimulates release of cytokines such as interleukin-6, interleukin-8 and tumour necrosis factor.[52 53] PM that reaches the most distal airways is phagocytosed in a dose-dependent manner by airway macrophages[54 55] (figure 5). Indeed, Kulkarni *et al*[56] reported that in healthy children, the amount of carbon in AM (as a marker of long-term personal exposure) is inversely associated with lung function. Phagocytosis of inhaled diesel PM by AM is also essential for normal removal of PM from the lungs, which minimises exposure of other airway cells. Conditions that impair AM phagocytosis will increase the proportion of PM impacting on and penetrating airway epithelial cells, further worsening the release of inflammatory mediators.[57–59] Indeed, a recent study found significantly lower amounts of diesel soot in AM, compatible with abnormal clearance of inhaled PM, in children with moderate-to-severe asthma compared with healthy controls—despite similar levels of personal exposure to black carbon.[60]
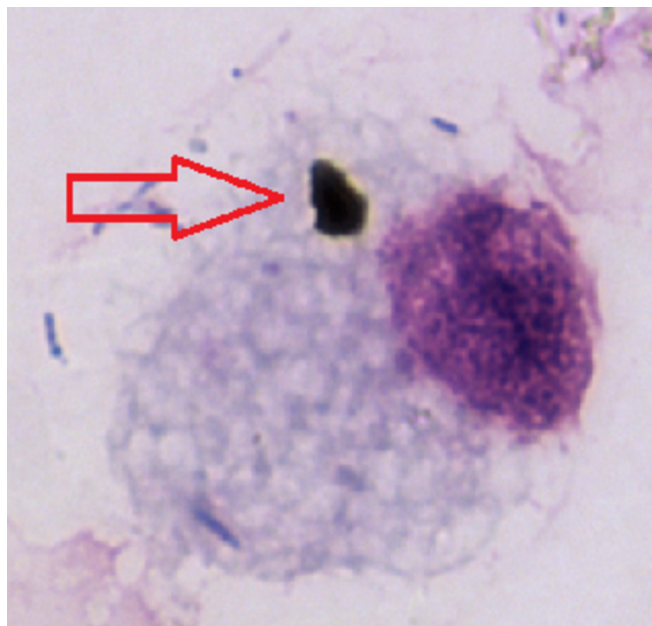
Figure 5 Phagocytosed black carbon (arrow) within an airway macrophage from a healthy child in one of the major cities in the UK.

Table 4 Advice on measures to take according to air pollution levels (adapted from British Lung Foundation website (https://www.blf.org.uk/support-for-you/air-pollution/what-can-i-do))

Pollution level	Measures
Low	► Avoid spending long periods of time along busy roads
Moderate	► Reduce or avoid strenuous outdoor activities
High	► Reduce or avoid strenuous outdoor activities ► Avoid pollution hotspots ► Avoid rush hours, travel earlier before pollution levels build up ► Use less polluted routes when cycling, walking or running ► Use of reliever inhaler if pollution is a trigger to asthma symptoms ► Seek medical attention

Increased exposure of airway epithelial cells to PM increases the potential for PM to translocate into the systemic circulation and directly cause adverse effects in distant organs, including the fetus where transplacental transfer of nanomaterials up to 240 nm is possible.[61]

WHAT CAN WE DO ABOUT DIESEL POLLUTION?
National level
In London, air pollution is mostly caused by road traffic, of which diesel vehicles are a major contributor, as discussed above. With an estimated 9400 premature deaths attributable to air pollution, it has the second biggest impact on public health.[19] These highly polluting vehicles should therefore be phased out to comply with legal limits of pollutants—and cleaner alternatives encouraged. Tougher national regulations on traffic emissions such as the expansion of Ultra Low Emission Zones and scrappage schemes for older generations of diesel vehicles should be considered. Indeed, the 2016 report from the Institute for Public Policy Research[23] estimated that phasing out diesel-powered vehicles in London would lead to large reductions in NO_X and NO_2 levels, ultimately lowering NO_2 levels to comply with EU standards. This report estimated that with a 45% reduction in NO_X and 56% reduction in NO_2, 1.4 million life-years would be gained along with a financial benefit of up to £800 million.

Planting trees can reduce air pollution by acting as a physical barrier to intercept PM and absorbing gaseous pollutants such as O_3,[62] although the effect on pollution concentrations at schools is, to date, unclear. However, the amount of pollutants removed by these organic barriers will be proportional to the extent of plantation.

Therefore, vast tall hedges around nurseries and schools should be encouraged, but this does not provide protection against pollution exposure during travel to and from schools.

Individual level
Various measures such as walking along less busy roads, cycling, use of public transport and carpooling may reduce exposure to air pollution,[63] but the evidence base for whether this is achievable over the long term, and is sufficient to improve health, is limited. The Department for Environment Food and Rural Affairs website provides information and forecast on UK air quality, while the British Lung Foundation provides information on various measures to take according to air pollution levels (table 4).

Air cleaning systems are available commercially claiming to reduce indoor pollution—these can either remove particles and gaseous pollutants or have ultraviolet light technology to destroy indoor pollutants.[64] All have their limitations, for example, large particles tend to settle before reaching filters, while gaseous pollutant filters may have short lifespans.[64] These systems also use electricity—which may not be from sustainable sources. Improvement in our air quality will benefit the whole population with lasting health and economic advantages. We should aim to build cities in order to promote and improve the health of the population.

In conclusion, in the UK, the phasing out of the current diesel car, van and taxi fleet, and replacing this fleet with greener alternatives must be a pillar of exposure-reduction strategy. Changes that would support such an initiative are (1) more active travel supported by better public transport infrastructure, (2) providing electric charging points on residential streets, and (3) providing clinicians with the tools to discuss personal exposure reduction strategies with their patients.

REFERENCES

1. Newby DE, Mannucci PM, Tell GS, *et al*. Expert position paper on air pollution and cardiovascular disease. *Eur Heart J* 2015;36:83–93.
2. Holegate S, Grigg J, Raymond A, *et al*. *Every breath we take: the lifelong impact of air pollution*, 2016.
3. Review of evidence on health aspects of air pollution—REVIHAAP Project. 2013.http://www.euro.who.int/__data/assets/pdf_file/0004/193108/REVIHAAP-Final-technical-report-final-version.pdf?ua=1
4. Chen Z, Salam MT, Eckel SP, *et al*. Chronic effects of air pollution on respiratory health in Southern California children: findings from the Southern California Children's Health Study. *J Thorac Dis* 2015;7:46–58.
5. Urman R, McConnell R, Islam T, *et al*. Associations of children's lung function with ambient air pollution: joint effects of regional and near-roadway pollutants. *Thorax* 2014;69:540–7.
6. Künzli N, McConnell R, Bates D, *et al*. Breathless in Los Angeles: the exhausting search for clean air. *Am J Public Health* 2003;93:1494–9.
7. Sources of air pollutants. *IARC monographs on the evaluation of carcinogenic risks to humans, No 109*, 2016.
8. Schauer JJ, Rogge WF, Hildemann LM, *et al*. Source apportionment of airborne particulate matter using organic compounds as tracers. *Atmos Environ* 1996;30:3837–55.
9. Nunes RAO, Alvim-Ferraz MCM, Martins FG, *et al*. Assessment of shipping emissions on four ports of Portugal. *Environ Pollut* 2017;231(Pt 2):1370–9.
10. Fuller GW, Tremper AH, Baker TD, *et al*. Contribution of wood burning to PM10 in London. *Atmos Environ* 2014;87:87–94.
11. Fuller G, Green D. Evidence for increasing concentrations of primary PM10 in London. *Atmos Environ* 2006;40:6134–45.
12. World Health Organization. WHO global urban ambient air pollution database. http://www.who.int/phe/health_topics/outdoorair/databases/cities/en/.
13. Department for Environment, Food and Rural Affairs. *UK Plan for tackling roadside nitrogen dioxide concentrations. Technical report*, 2017.
14. Air Quality Expert Group. *Nitrogen dioxide in the United Kingdom*, 2004.
15. *New Car CO2 Report 2017*. 16th edn, 2017.
16. Anenberg SC, Miller J, Minjares R, *et al*. Impacts and mitigation of excess diesel-related NO$_x$ emissions in 11 major vehicle markets. *Nature* 2017;545:467–71.
17. Reşitoğlu İbrahim Aslan, Altinişik K, Keskin A. The pollutant emissions from diesel-engine vehicles and exhaust aftertreatment systems. *Clean Technol Environ Policy* 2015;17:15–27.
18. Environmental Committee London Assembly. *Driving away from diesel: reducing air pollution from diesel vehicles*, 2015.
19. Quilter-Pinner H, Laybourn-Langton L. *Lethal and illegal: London's air pollution crisis*: IPPR, 2016.
20. Internation Agency for Research on Cancer WHO. *IARC: diesel engine exhaust carcinogenic*, 2012.
21. Air Quality Guidelines for Europe. *WHO regional publications, European Series*, 2000. No. 91.
22. Greenpeace. More than 1,000 nurseries nationwide close to illegally polluted roads. 2017. https://unearthed.greenpeace.org/2017/04/04/air-pollution-nurseries/
23. Laybourn-Langton L, Quilter-Pinner H, Ho H. *Lethal and Illegal: solving London's Air Pollution Crisis*, 2016.
24. Morales E, Garcia-Esteban R, de la Cruz OA, *et al*. Intrauterine and early postnatal exposure to outdoor air pollution and lung function at preschool age. *Thorax* 2015;70:64–73.
25. Proietti E, Röösli M, Frey U, *et al*. Air pollution during pregnancy and neonatal outcome: a review. *J Aerosol Med Pulm Drug Deliv* 2013;26:9–23.
26. Pedersen M, Giorgis-Allemand L, Bernard C, *et al*. Ambient air pollution and low birthweight: a European cohort study (ESCAPE). *Lancet Respir Med* 2013;1:695–704.
27. European Commission. Air Quality Standards. http://ec.europa.eu/environment/air/quality/standards.htm.
28. Carrillo G, Perez Patron MJ, Johnson N, *et al*. Asthma prevalence and school-related hazardous air pollutants in the US–México border area. *Environ Res* 2018;162:41–8.
29. Lee JY, Leem JH, Kim HC, *et al*. Effects of traffic-related air pollution on susceptibility to infantile bronchiolitis and childhood asthma: a cohort study in Korea. *J Asthma* 2018;55:223–30.
30. Girguis MS, Strickland MJ, Hu X, *et al*. Exposure to acute air pollution and risk of bronchiolitis and otitis media for preterm and term infants. *J Expo Sci Environ Epidemiol* 2017.
31. Hwang BF, Chen YH, Lin YT, *et al*. Relationship between exposure to fine particulates and ozone and reduced lung function in children. *Environ Res* 2015;137:382–90.
32. Gauderman WJ, Urman R, Avol E, *et al*. Association of improved air quality with lung development in children. *N Engl J Med* 2015;372:905–13.
33. Gasana J, Dillikar D, Mendy A, *et al*. Motor vehicle air pollution and asthma in children: a meta-analysis. *Environ Res* 2012;117:36–45.
34. Krämer U, Koch T, Ranft U, *et al*. Traffic-related air pollution is associated with atopy in children living in urban areas. *Epidemiology* 2000;11:64–70.
35. Morgenstern V, Zutavern A, Cyrys J, *et al*. Atopic diseases, allergic sensitization, and exposure to traffic-related air pollution in children. *Am J Respir Crit Care Med* 2008;177:1331–7.
36. Pénard-Morand C, Raherison C, Charpin D, *et al*. Long-term exposure to close-proximity air pollution and asthma and allergies in urban children. *Eur Respir J* 2010;36:33–40.
37. Bouazza N, Foissac F, Urien S, *et al*. Fine particulate pollution and asthma exacerbations. *Arch Dis Child* 2017:archdischild-2017-312826.
38. Hasunuma H, Yamazaki S, Tamura K, *et al*. Association between daily ambient air pollution and respiratory symptoms in children with asthma and healthy children in western Japan. *J Asthma* 2018;7:1–7.
39. Basagaña X, Esnaola M, Rivas I, *et al*. Neurodevelopmental deceleration by urban fine particles from different emission sources: a longitudinal observational study. *Environ Health Perspect* 2016;124:1630–6.
40. Saenen ND, Plusquin M, Bijnens E, *et al*. In utero fine particle air pollution and placental expression of genes in the brain-derived neurotrophic factor signaling pathway: an ENVIRONAGE Birth Cohort Study. *Environ Health Perspect* 2015;123:834–40.
41. Bos I, De Boever P, Int Panis L, *et al*. Physical activity, air pollution and the brain. *Sports Med* 2014;44:1505–18.
42. Pujol J, Martínez-Vilavella G, Macià D, *et al*. Traffic pollution exposure is associated with altered brain connectivity in school children. *Neuroimage* 2016;129:175–84.
43. Thiering E, Cyrys J, Kratzsch J, *et al*. Long-term exposure to traffic-related air pollution and insulin resistance in children: results from the GINIplus and LISAplus birth cohorts. *Diabetologia* 2013;56:1696–704.
44. Risnes KR, Vatten LJ, Baker JL, *et al*. Birthweight and mortality in adulthood: a systematic review and meta-analysis. *Int J Epidemiol* 2011;40:647–61.
45. Calderón-Garcidueñas L, Vincent R, Mora-Tiscareño A, *et al*. Elevated plasma endothelin-1 and pulmonary arterial pressure in children exposed to air pollution. *Environ Health Perspect* 2007;115:1248–53.
46. Bilenko N, van Rossem L, Brunekreef B, *et al*. Traffic-related air pollution and noise and children's blood pressure: results from the PIAMA birth cohort study. *Eur J Prev Cardiol* 2015;22:4–12.
47. Sram RJ, Veleminsky M, Veleminsky M, *et al*. The impact of air pollution to central nervous system in children and adults. *Neuro Endocrinol Lett* 2017;38:389–96.
48. Forns J, Dadvand P, Esnaola M, *et al*. Longitudinal association between air pollution exposure at school and cognitive development in school children over a period of 3.5 years. *Environ Res* 2017;159:416–21.
49. Pye S, King K, Sturman J. *Air quality and social deprivation in the UK: an environmental inequalities analysis—final report to Defra*, 2006.

50. Wise J. UK survey confirms link between deprivation and smoking. *BMJ* 2014;348:g2184.

51. Anderson JO, Thundiyil JG, Stolbach A. Clearing the air: a review of the effects of particulate matter air pollution on human health. *J Med Toxicol* 2012;8:166–75.

52. Rylance J, Fullerton DG, Scriven J, *et al*. Household air pollution causes dose-dependent inflammation and altered phagocytosis in human macrophages. *Am J Respir Cell Mol Biol* 2015;52:584–93.

53. Imrich A, Ning Y, Lawrence J, *et al*. Alveolar macrophage cytokine response to air pollution particles: oxidant mechanisms. *Toxicol Appl Pharmacol* 2007;218:256–64.

54. Boylen CE, Sly PD, Zosky GR, *et al*. Physiological and inflammatory responses in an anthropomorphically relevant model of acute diesel exhaust particle exposure are sex and dose-dependent. *Inhal Toxicol* 2011;23:906–17.

55. Saxena RK, Gilmour MI, Hays MD. Isolation and quantitative estimation of diesel exhaust and carbon black particles ingested by lung epithelial cells and alveolar macrophages in vitro. *Biotechniques* 2008;44:799–805.

56. 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.

57. Geiser M, Stoeger T, Casaulta M, *et al*. Biokinetics of nanoparticles and susceptibility to particulate exposure in a murine model of cystic fibrosis. *Part Fibre Toxicol* 2014;11:19.

58. Becker S, Dailey L, Soukup JM, *et al*. TLR-2 is involved in airway epithelial cell response to air pollution particles. *Toxicol Appl Pharmacol* 2005;203:45–52.

59. Jeannet N, Fierz M, Schneider S, *et al*. Acute toxicity of silver and carbon nanoaerosols to normal and cystic fibrosis human bronchial epithelial cells. *Nanotoxicology* 2016;10:279–91.

60. Brugha RE, Mushtaq N, Round T, *et al*. Carbon in airway macrophages from children with asthma. *Thorax* 2014;69:654–9.

61. Wick P, Malek A, Manser P, *et al*. Barrier capacity of human placenta for nanosized materials. *Environ Health Perspect* 2010;118:432–6.

62. Nowak DJ, Hirabayashi S, Bodine A, *et al*. Tree and forest effects on air quality and human health in the United States. *Environ Pollut* 2014;193:119–29.

63. Sá TH, Tainio M, Goodman A, *et al*. Health impact modelling of different travel patterns on physical activity, air pollution and road injuries for São Paulo, Brazil. *Environ Int* 2017;108:22–31.

64. United States Environmental Protection Agency. *Guide to air cleaners in the home*, 2008.