Effects of air pollution exposure on child health and do interventions work?

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1. Introduction

There are significant impacts from air pollution on physical health, both in children and in adults. Of note a number of the health effects in adults are actually the end result of exposure at a young age. Therefore, reducing air pollution exposure for children would have a likely improvement in the health of those individuals as adults. This review will look at the physical health effects on children. It will then review the current literature surrounding the possible improvements that can be made through reductions in air pollution exposure through interventions.

2. Air pollution health effects in children

While the effects of air pollution exposure are seen at all ages, the exposure prior to birth is also important, particularly in the second and third trimesters when organs such as the lungs and brain undergo significant change [1].

Lung development

Adverse effects on lung growth start during the vital phases of lung growth and development in the third trimester [2]. Therefore, it is important to take in to account maternal exposures during pregnancy. Recent studies have shown that exposure to particulate matter (PM) in pregnancy can result in small particles travelling to the placenta and thus having potential direct effect on the fetus [3]. The likely effect is that this then results in placental insufficiency meaning that the placenta is unable to provide the correct amount of support to the growing fetus [4].

Studies have shown that maternal PM exposure is associated with effects on the newborn including low birth weight and preterm delivery [5]. These in themselves will affect lung growth and development both prior to and after birth. For example; alveolar development happens relatively late on (after 24 weeks' gestation) and alveolar growth does not complete until the teenage years. This could be the starting point of long-term effects on lung growth and function and should be considered a vital time for interventions.

Lung function

Lung function testing is used clinically to assess how well the lungs are working, and whether medication is effective. In terms of pollution exposure, it gives us some very interesting information both of current and long-term exposure and potentially on the impacts of interventions.

Lung function (as measured by FEV_1 (Forced Expiratory Volume in 1 second) and FVC (Forced Vital Capacity)) is lower in children exposed to high levels of pollutants [6-10]. The adverse effects persist into adulthood and many never reach their full lung function potential [11]. It also does not appear to matter how you define high exposure, whether by direct monitoring or just living within 100m of a major road or highway or living within a city with high background PM levels [12].

Respiratory symptoms

There are numerous studies which demonstrate the associations between PM and NO_2 exposure and asthma exacerbations or worse asthma symptoms [6, 7, 13-17]. More recently there has been discussion around whether exposure in early life may result in a child being more likely to develop asthma in the first place. For example; McConnell *et al.* found children in southern California were more likely to develop asthma if they had higher exposures to air pollution (modelled exposure at the home and school), with the effect most accentuated with NO_2 exposure [18]. However, the European Study of Cohorts for Air Pollution Effects (ESCAPE) study in Europe found no significant association between air pollution exposure and childhood asthma prevalence [19].

All current published studies do agree that pollution exposure results in more frequent asthma exacerbations, increased hospitalisations due to wheezing and respiratory symptoms and even respiratory infections such as pneumonia. The meta-analysis carried out within the ESCAPE birth cohorts also found a significant association between PM_{10} and NO_2 and pneumonia prevalence, as well as increased risk of otitis media [20]. These effects also appear to be present with indoor air pollutants; a meta-analysis by Lin *et al.* found that gas cooking increased the risk of both asthma prevalence and risk of wheezing [21].

Other health effects in children

Cardiovascular

While the main cardiovascular health effects of air pollution exposure are most commonly seen in adults it is highly likely that these start in childhood. Cuttica *et al.* [22] reported that the combined effects of air pollution on the cardiovascular and pulmonary systems in children increase the risk of left ventricular hypertrophy and poorer cardiac function of the left side of the heart. These effects may be exacerbated by changes in blood pressure due to long-term exposure to NO_2 and $PM_{2.5}$ [23]. Other effects such as atherosclerosis also appear to start early in life [24].

Development

Newer studies are reporting emerging associations between exposure and neurodevelopmental and cognitive effects. For example, Raz *et al.* [25] demonstrated that $PM_{2.5}$ exposure during pregnancy is associated with an increased risk of the child developing autism particularly with third trimester exposure. The widespread impact on the developing brain is supported by evidence from a meta-analysis from six European birth cohort studies [26] that demonstrated that NO_2 exposure during pregnancy resulted in delayed psychomotor development in early childhood.

Diabetes

There are an increasing number of studies demonstrating that air pollution exposure also has a part to play in the development of diabetes (primarily type 2 diabetes). Long term exposure to PM and NO_2 is associated with a significantly elevated risk of type 2 diabetes [27], along with an increased risk of insulin resistance in children which may in the long-term result in type 2 diabetes [28].

Cancer

There is still limited evidence in relation to the risk of childhood cancers resulting from air pollution exposure. Heck *et al.* [29] found associations between traffic related air pollution (during pregnancy) and several cancers including Acute Lymphoblastic Leukaemia (ALL), Germ cell tumours such as teratomas and retinoblastomas. Further work is required to fully investigate these associations.

3. Assessment of air pollution exposure

In order to assess the impact of an intervention to reduce air pollution exposure, there is a need to have accurate assessment of the exposure levels, either on a personal and area-based method

Assessment of exposure to air pollution may be divided in to three main categories, each with strengths and limitations and the final choice depends very much on the intervention being assessed;

i) Computer modelling
ii) Directly monitored or "personal monitoring"
iii) Biomarkers of exposure

Brauer *et al.* proposes a hierarchy of pollution exposure assessment for use in epidemiological studies (Figure 1) [30].

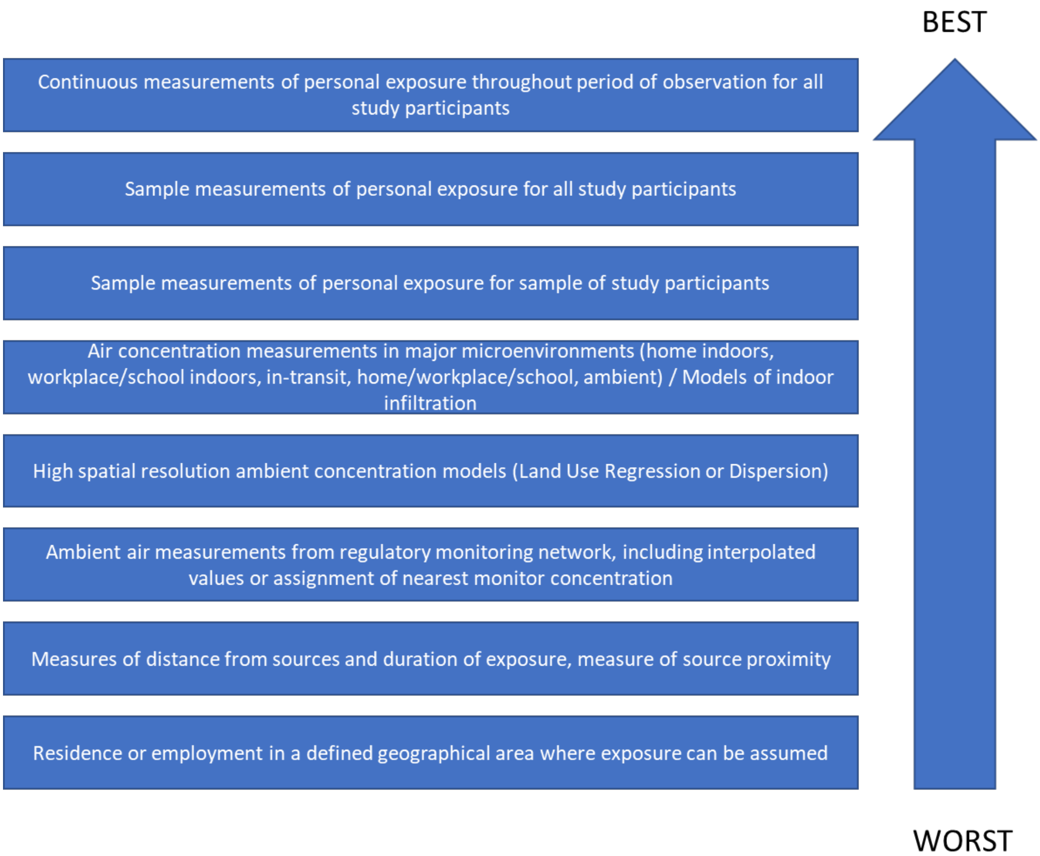

Figure 1 Hierarchy of Assessment of Exposure adapted from Brauer et al. [30].

Ideally each participant would have continuous individual monitoring for the entirety of the study. This is however not practical if looking at long term exposures. However it could be used in two periods of "normal activity" monitoring before and after the intervention. Longer term exposures would more likely need fixed monitors and the inclusion of computer pollution models.

Computer modelled pollution exposure

Computer models often take into account fixed monitors they do not exclusively rely on that data and therefore can provide results for areas without fixed monitors as demonstrated in the following models;

i) For the Avon Longitudinal Study of Parents and Children in Bristol, the ADMS-Urban (for local exposure) and NAME-III (regional/long range) models were used for short term measures of pollution exposure combined with multiple other data sources to provide a complete model of exposure over a set time period [31].

ii) London Air Quality Toolkit (Kings College University) provides an emissions dispersion model based on local fixed monitoring sites in the short-term while also taking into account annual means at the same site. These data are then extrapolated to provide a modelled exposure over a certain time period at any postcode within the London area [32]. This model has been used in various pollution-based studies in conjunction with other methods of pollution exposure measurement [32-40].

Pierse *et al.* [41] used the Airviro dispersion model (for the home address) to look at the effects of air pollution (primary PM from roads) exposure on respiratory symptoms in Leicester from 1998-2001. Airviro provides a PM_{10} reading for an address using models of traffic flow and wind direction/speed without the need for fixed monitors.

Fixed monitors

In comparison, the Children's Health Study in California [8] used hourly or daily concentrations of NO_2, $PM_{2.5}$ and PM_{10} taken from Federal Equivalent Method or Equivalent instrumentation (fixed monitors) in each of the communities enrolled in the study. While this may result in a delay in receiving the results as the data will need to be cleaned post collection. It does however provide local individual results which account for acute unexpected variations (such as a storm). Fixed monitors are also useful when the intervention is in a fixed space or room and therefore monitoring of that space will be useful.

Personal monitoring

Personal monitoring is a potential gold standard, since this allows for each individual to be monitored for a time period (usually 24-48 hours) with PM and NO_2 monitors being used the most frequently.

Personal monitoring is best suited to relatively short time periods, providing a snapshot, and is most useful if the participant has a regular routine (such as school children). Monitoring equipment varies greatly, with size and weight being a significant consideration, particularly when carrying out studies with children. The Microaeth is a lightweight monitor which allows for 24 hours of monitoring and previous studies have shown correlation with markers of airway inflammation such as FeNO in a cohort in Manhatten [42] and airway macrophage black carbon in cyclists in London [43].

This methodology is most useful in studies of short-term outcomes, such as studies linking exposure with acute respiratory symptoms or biomarkers.

Airway macrophage black carbon

While monitoring and models tell us a great deal about how much a person is exposed to – they can not quantify how much an individual breathes in, as this is dependent on various factors (lung function, lung capacity, illness, exercise levels).

Airway Macrophage Black Carbon (AMBC) is a marker of how much an individual breathes in and therefore is useful as a marker of whether and intervention has reduced pollution levels. AMBC is assessed through sampling of cells from the lower airway (usually through sputum induction).

Several studies have been carried out using varying methods to assess AMBC. All the reported studies use light microscopy to assess BC loading. The least precise method of simply reporting the percentage of cells that contained BC was reported by Bunn *et al.* in 2001 [44]. A further method was then proposed by Kalappanavar *et al.* in 2012 [45] in which macrophages were graded 1-4 in terms of their carbon loading, although this tended to be imprecise and very operator dependent.

The most widely used method is to assess the mean or median area of black particles per macrophage per subject. This method has been used in several different studies – but with slightly different methodology between studies. All studies reported a relationship between their external measure of exposure (modelled or personal monitoring) and the mean AMBC [43, 46-51].

Further validation of AMBC is its link with clinically relevant health effects. For example, Kulkarni *et al.* [49] found that asthmatic children had lower levels of AMBC than healthy children a finding confirmed by Brugha *et al.* in 2014 with this study showing that children with moderate to severe asthma had 51% lower levels of AMBC compared to healthy controls [33], it is possible this is due to impaired phagocytosis in asthma or a treatment effect of inhaled corticosteroids and is an area that requires more investigation.

4. Effect of Interventions

Different interventions are suggested to try and reduce pollution levels;

- Large-scale interventions
  - Those targeting traffic related air pollution
    - Congestion charging zones
    - Road closures/Non-idling zones
    - Vehicle bans
    - Electric Vehicle promotion
  - Industry regulation of industry related sources
    - Power plant standards and fuel conversion
    - Reduction in number of factories
  - Building Regulations
    - Sites for schools/care homes and other buildings designed to support the vulnerable should be considered and moved away from busy roads if possible.
- Mid-scale interventions
  - Cooking/stove interventions
    - Change in stoves
    - Wood-burning stove bans
- Small-scale interventions / Personal interventions
  - Air purifiers
  - Alteration in route to school/work
  - Education interventions
  - Green walls
  - Citizen science interventions

The following section summarises a number of studies in which interventions have been made that have then directly affected children's health. These studies have been carried out in different countries across the world and therefore impacts need to be considered in relation to current pollution levels. While there are numerous studies looking at the impact on pollution levels themselves, studies with the impact on health outcomes are much more limited.

Southern California – The Children's Health Study

Methods

The results reported by *Gauderman et al.* demonstrates the effects of a reduction in pollution levels due to aggressive anti-pollution reduction strategies in Southern California over a 13 year period. In particular the Los Angeles basin provided a natural landscape that trapped pollution emitted by the extremely large road traffic fleet, significant industrial processes and an extremely large seaport. The anti-pollution strategies included ways of controlling both traffic and industry related pollution and combined this with fuel and consumer-product reformulations.

Impacts of reduction in air pollution levels

In the community with the highest levels of air pollution the $PM_{2.5}$ 4-year mean declined from 31.5µg per cubic meter to 17.8µg per cubic meter in one of the cohorts, a 43% reduction. Similar reductions were seen in each of the other 4 cohorts. This reduction in air pollution levels was associated with a reduction in the number of children with significantly low FEV1. Over the period the number of children at age 15 with clinically low FEV_1 (<80% predicted) dropped from 7.9% to 3.6% [52].

Effect of green space on asthma risk

Methods

Feng et al. looked at cross-sectional data of children in Australia diagnosed with asthma. Specifically looking at the association between asthma symptoms and exposure to heavy traffic levels. They then looked at whether green space was protective against the risk of asthma symptoms.

Results

In children exposed to high traffic volumes the odds ratio of asthma symptoms was 1.87 (95% CI 1.37 to 2.55). Whereas in children living in areas with over 40% green space the odds ratio was only 0.32 (95% CI 0.12 to 0.84). Therefore suggesting that those children that live with more green space are less likely to have asthma and exacerbations due to the buffering of the effect of green space on high levels of air pollution [53].

Air Purifiers in Schools in Beijing [54]

Methods

Ionising air purifiers were place in classrooms in several schools in Beijing. Mixed-effect models were used to establish associations between exposures and health parameters. This was a randomised double-blind study, in which placebo purifiers were used in some of the classrooms. 44 children were included in the study.

Impact

$PM_{0.5}$, $PM_{2.5}$, PM_{10} and BC were decreased by 48%, 44%, 34% and 50%, respectively, there was no effect on O_3 levels. In the children where there was a reduction in air pollution levels there was an increase in FEV_1 of 4.4% and a reduction in FeNO (fractional exhaled nitrogen oxide, a marker of asthma related inflammation) of 14.7%.

Air purifiers in schools in Korea [55]

Methods

Air purifiers were placed in classrooms of schools and children with asthma were recruited. Placebo purifiers were used in half of the schools.

Results

30 children were recruited to the study. Mean $PM_{2.5}$ was significantly higher in the placebo group (17.0 $\mu g/m^3$) than in the true air purifier group (9.26 $\mu g/m^3$). The only result with a significant difference between groups was in the medication score (a score based on use of reliever and acute medications). There was no difference in lung function between the groups.

School Inner-City Asthma Intervention Study – Boston USA [56]

Methods

Randomised, blinded, placebo-controlled school intervention study to examine whether integrated pest management +/- air purifiers will result in improved asthma control and symptoms. Study still recruiting at present. Primary outcome will be asthma symptoms during the school year.

Sample Size analysis

They will recruit 300 participants (with an expected drop-out rate on 60 participants) allowing for a total of 240 participants at the end of the study. They will have an 80% power to detect a difference of at least 0.6 days of symptoms and > 90% power to detect a difference of 0.75 days between the two groups.

Atlanta Olympics [57]

Methods

In 1996 multiple policies were put in to reduce air pollution levels and improve air quality on a city-wide basis. They looked at emergency department visits through this period alongside the ozone (O_3) levels.

Results

While there was a 30% reduction in ozone levels across the 4-week period compared to the prior 4 weeks, there was no impact on emergency department activity.

Beijing Olympics[58]

Methods

During the Beijing Olympics, the pollution levels within the city were drastically reduced through city wide initiatives, including banning cars on specific days of the week. Therefore resulting in a natural experiment that could be used to look at the impact on fetal growth.

Results

These short term decreases in air pollution levels late in pregnancy (ie those babies that were born in the 1-3 months post the Olympic time period had significant effects on birth weight. Those babies born in this time period had higher birth weights compared to those born in the corresponding month the year before.

5. Impact Table

Suggested impact of improved air quality	Result from study - Assume Study Runs over 12 months
Lung Function FEV_1	If air pollution level can halve then would expect to see 20-50% reduction in the number of children with significantly low FEV_1 Based on the California Health Study
Unscheduled medical attendances (for example GP or A+E attendance)	If particulate levels halve, would expect this to have a 20-50% reduction on the need for USME's The emerging evidence from the COVID-19 situation within London is that Asthma exacerbations have all but disappeared during lockdown.
Inhaler Use (blue reliever use)	If air purifiers are effective at reducing particle and allergens within the school environment, it would be likely to reduce blue inhaler use due to this to 0. Children may still have trigger such as exercise and viral infections

6. Discussion

There is myriad of evidence and research demonstrating the associations between air pollution exposure and significant health effects in children. Some of the most demonstrable are the respiratory associations. This is because the inhalation of small particles exacerbates asthma, poor lung function and allergies in the short term. The Oxford street study is a prime example of this, walking down a busy polluted road results in significant impacts on lung function when compared to walking through a leafy green park in London [59]. Exposure to high levels for long periods on a daily basis (such as growing up in a busy polluted city) also increases your risk of developing asthma and your risk of severe infections such pneumonia. Other health effects such as those to do with the cardiovascular system and cancer which are more evident in adults begin during childhood and therefore childhood is a prime time to address these risks and try to reduce the impact of exposure. A complicating factor for this is that children are reliant on adults to make choices for them and their peers. Additionally there is a wealth of evidence both from real-life and laboratory based studies which inform how these health effects occur through the effect on the immune system.

Where the evidence is lacking is how we can alter these health effects. This is in part due to the fact that to reduce pollution levels requires policy and governments to act, but also that it takes a prolonged period to reduce pollution levels. The next complicating factor is that causality and association in these situations is extremely difficult to prove. We do know from unexpected reductions (such as impact of local policies during the Olympics) the pollution levels can drop significantly. The impact on health is less clear. The best evidence to date is the Children's Health Study in California, which demonstrated a clear reduction in the number of children with significantly low lung function when the air quality improved.

There are clear results on pollution reduction from small scale intervention studies, where air purifiers have dropped particle levels significantly in schools and work-places. However, the associated health effects are not as clear. What is currently needed is a study that examines the impact of air pollution reduction on a local scale on respiratory function and symptoms on a large scale.

1. Party, R.o.a.W., *Every breath we take: the lifelong impact of air pollution*. 2016.
2. Goldizen, F.C., P.D. Sly, and L.D. Knibbs, *Respiratory effects of air pollution on children.* Pediatr Pulmonol, 2015.
3. Bové, H., et al., *Ambient black carbon particles reach the fetal side of human placenta.* Nature Communications, 2019. **10**(1): p. 1-7.
4. van den Hooven, E.H., et al., *Air pollution exposure and markers of placental growth and function: the generation R study.* Environ Health Perspect, 2012. **120**(12): p. 1753-9.
5. Ha, S., et al., *The effects of air pollution on adverse birth outcomes.* Environ Res, 2014. **134**: p. 198-204.
6. Anderson, J.O., J.G. Thundiyil, and A. Stolbach, *Clearing the air: a review of the effects of particulate matter air pollution on human health.* J Med Toxicol, 2012. **8**(2): p. 166-75.
7. Chen, Z., 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**(1): p. 46-58.
8. Gauderman, W.J., *Association between Air Pollution and Lung Function, Growth in Southern California Children.* Am J Respir Crit Care Med, 2000.
9. Grigg, J., *Traffic-derived air pollution and lung function growth.* Am J Respir Crit Care Med, 2012. **186**(12): p. 1208-9.
10. Rice, M.B., et al., *Lifetime Exposure to Ambient Pollution and Lung Function in Children.* Am J Respir Crit Care Med, 2015.
11. Gauderman, W.J., et al., *The effect of air pollution on lung development from 10 to 18 years of age.* N Engl J Med, 2004. **351**(11): p. 1057-67.
12. Hwang, B.F., et al., *Relationship between exposure to fine particulates and ozone and reduced lung function in children.* Environ Res, 2015. **137**: p. 382-90.
13. Balmes, J., *How does diesel exhaust impact asthma?* 2011.
14. Barnett, A.G., et al., *Air pollution and child respiratory health: a case-crossover study in Australia and New Zealand.* Am J Respir Crit Care Med, 2005. **171**(11): p. 1272-8.
15. Berhane, K., et al., *The effect of ambient air pollution on exhaled nitric oxide in the Children's Health Study.* Eur Respir J, 2011. **37**(5): p. 1029-36.
16. Brauer, M., et al., *Air pollution and development of asthma, allergy and infections in a birth cohort.* Eur Respir J, 2007. **29**(5): p. 879-88.
17. Cai, J., et al., *Acute effects of air pollution on asthma hospitalization in Shanghai, China.* Environ Pollut, 2014. **191**: p. 139-44.
18. McConnell, R., et al., *Childhood incident asthma and traffic-related air pollution at home and school.* Environ Health Perspect, 2010. **118**(7): p. 1021-6.
19. Molter, A., et al., *A multicentre study of air pollution exposure and childhood asthma prevalence: the ESCAPE project.* Eur Respir J, 2015. **45**(3): p. 610-24.
20. MacIntyre, E.A., et al., *Air pollution and respiratory infections during early childhood: an analysis of 10 European birth cohorts within the ESCAPE Project.* Environ Health Perspect, 2014. **122**(1): p. 107-13.
21. Lin, W., B. Brunekreef, and U. Gehring, *Meta-analysis of the effects of indoor nitrogen dioxide and gas cooking on asthma and wheeze in children.* Int J Epidemiol, 2013. **42**(6): p. 1724-37.
22. Cuttica, M.J., et al., *Loss of Lung Health from Young Adulthood and Cardiac Phenotypes in Middle Age.* Am J Respir Crit Care Med, 2015. **192**(1): p. 76-85.

23. Bilenko, N., 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**(1): p. 4-12.
24. Kaufman, J.D., et al., *Prospective study of particulate air pollution exposures, subclinical atherosclerosis, and clinical cardiovascular disease: The Multi-Ethnic Study of Atherosclerosis and Air Pollution (MESA Air).* Am J Epidemiol, 2012. **176**(9): p. 825-37.
25. Raz, R., et al., *Autism spectrum disorder and particulate matter air pollution before, during, and after pregnancy: a nested case-control analysis within the Nurses' Health Study II Cohort.* Environ Health Perspect, 2015. **123**(3): p. 264-70.
26. Guxens, M., et al., *Air pollution during pregnancy and childhood cognitive and psychomotor development: six European birth cohorts.* Epidemiology, 2014. **25**(5): p. 636-47.
27. Wang, B., et al., *Effect of long-term exposure to air pollution on type 2 diabetes mellitus risk: a systemic review and meta-analysis of cohort studies.* Eur J Endocrinol, 2014. **171**(5): p. R173-82.
28. Thiering, E., 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**(8): p. 1696-704.
29. Heck, J.E., et al., *Childhood cancer and traffic-related air pollution exposure in pregnancy and early life.* Environ Health Perspect, 2013. **121**(11-12): p. 1385-91.
30. Brauer M, A., Buzzelli, Henderson, Larson, Marshall, Nethery, Steyn and Su, *Models of Exposure for Use in Epidemiological Studies of Air Pollution Health Impacts | SpringerLink*, in *Air Pollution Modeling and Its Application XIX*, M.A.I. Borrego C., Editor. 2008, SpringerLink: NATO Science for Peace and Security Series Series C. p. 589-604.
31. Gulliver, J., et al., *Local- and regional-scale air pollution modelling (PM10) and exposure assessment for pregnancy trimesters, infancy, and childhood to age 15years: Avon Longitudinal Study of Parents And Children (ALSPAC).* Environ Int, 2018. **113**: p. 10-19.
32. Kelly, F., et al., *The impact of the congestion charging scheme on air quality in London. Part 1. Emissions modeling and analysis of air pollution measurements.* Res Rep Health Eff Inst, 2011(155): p. 5-71.
33. Brugha, R.E., et al., *Carbon in airway macrophages from children with asthma.* Thorax, 2014. **69**(7): p. 654-9.
34. Walton, R.T., et al., *Air pollution, ethnicity and telomere length in east London schoolchildren: An observational study.* Environ Int, 2016. **96**: p. 41-47.
35. Barratt, B. and J.K. Quint, *Asthma hospitalisations and air pollution.* Thorax, 2016. **71**(12): p. 1076-1077.
36. Lee, M., et al., *Corrigendum to "Land use regression modelling of air pollution in high density high rise cities: A case study in Hong Kong" [Sci. Total Environ. 592 (2017) 306-315].* Sci Total Environ, 2017. **603-604**: p. 832-833.
37. Butland, B.K., et al., *Air pollution and the incidence of ischaemic and haemorrhagic stroke in the South London Stroke Register: a case-cross-over analysis.* J Epidemiol Community Health, 2017. **71**(7): p. 707-712.
38. Lee, M., et al., *Land use regression modelling of air pollution in high density high rise cities: A case study in Hong Kong.* Sci Total Environ, 2017. **592**: p. 306-315.

39. Krauskopf, J., et al., *The human circulating miRNome reflects multiple organ disease risks in association with short-term exposure to traffic-related air pollution.* Environ Int, 2018. **113**: p. 26-34.
40. Tang, R., et al., *Integrating travel behavior with land use regression to estimate dynamic air pollution exposure in Hong Kong.* Environ Int, 2018. **113**: p. 100-108.
41. Pierse, N., et al., *Locally generated particulate pollution and respiratory symptoms in young children.* Thorax, 2006. **61**(3): p. 216-20.
42. Lovinsky-Desir, S., et al., *Physical activity, black carbon exposure and airway inflammation in an urban adolescent cohort.* Environ Res, 2016. **151**: p. 756-762.
43. Nwokoro, C., et al., *Cycling to work in London and inhaled dose of black carbon.* Eur Respir J, 2012. **40**(5): p. 1091-7.
44. Bunn, H.J., et al., *Ultrafine particles in alveolar macrophages from normal children.* Thorax, 2001. **56**(12): p. 932-4.
45. Kalappanavar, N.K., et al., *Carbon particles in airway macrophage as a surrogate marker in the early detection of lung diseases.* Int J Occup Environ Med, 2012. **3**(2): p. 68-75.
46. Bai, Y., et al., *Carbon loading in airway macrophages as a biomarker for individual exposure to particulate matter air pollution - A critical review.* Environ Int, 2014. **74C**: p. 32-41.
47. Fullerton, D.G., et al., *Biomass fuel use and indoor air pollution in homes in Malawi.* Occup Environ Med, 2009. **66**(11): p. 777-83.
48. Jacobs, L., et al., *Air pollution related prothrombotic changes in persons with diabetes.* Environ Health Perspect, 2010. **118**(2): p. 191-6.
49. Kulkarni, N., et al., *Carbon in airway macrophages and lung function in children.* N Engl J Med, 2006. **355**(1): p. 21-30.
50. Kulkarni, N.S., et al., *Carbon loading of alveolar macrophages in adults and children exposed to biomass smoke particles.* Sci Total Environ, 2005. **345**(1-3): p. 23-30.
51. Nwokoro, C., R. Brugha, and J. Grigg, *Alveolar macrophages carbon load: a marker of exposure?* Eur Respir J, 2013. **41**(3): p. 763.
52. Gauderman, W.J., et al., *Association of improved air quality with lung development in children.* N Engl J Med, 2015. **372**(10): p. 905-13.
53. X., F. and B. Astell, *Is Neighborhood Green Space Protective Against Associations Between Child Asthma, Neighborhood Traffic Volume and Perceived Lack of Area Safety? Multilevel Analysis of 4447 Australian Children.* International journal of environmental research and public health, 2017. **14**(5).
54. W., D., et al., *Different Cardiorespiratory Effects of Indoor Air Pollution Intervention With Ionization Air Purifier: Findings From a Randomized, Double-Blind Crossover Study Among School Children in Beijing.* Environmental pollution (Barking, Essex : 1987), 2019. **254**(Pt B).
55. Dh, et al., *Effects of Indoor Air Purifiers on Children With Asthma.* Yonsei medical journal, 2020. **61**(4).
56. Ps, et al., *The School Inner-City Asthma Intervention Study: Design, Rationale, Methods, and Lessons Learned.* Contemporary clinical trials, 2017. **60**.
57. L., P.J., et al., *Impact of Improved Air Quality During the 1996 Summer Olympic Games in Atlanta on Multiple Cardiovascular and Respiratory Outcomes.* Research report (Health Effects Institute), 2010(148).

58. Q., R.D., et al., *Differences in Birth Weight Associated With the 2008 Beijing Olympics Air Pollution Reduction: Results From a Natural Experiment*. Environmental health perspectives, 2015. **123**(9).

59. Sinharay, R., et al., *Respiratory and cardiovascular responses to walking down a traffic-polluted road compared with walking in a traffic-free area in participants aged 60 years and older with chronic lung or heart disease and age-matched healthy controls: a randomised, crossover study*. Lancet, 2018. **391**(10118): p. 339-349.

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