Air Pollutants and Attention Deficit Hyperactivity Disorder Medication Administration in Elementary Schools

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Abstract

Introduction. Air pollution is considered a risk factor for several diseases, including respiratory and cardiovascular. However, the effects of air pollution on neurobehavioral disorders is not confirmed yet. Thus, this study aimed at determining the association of seven air pollutants with ADHD medication administration (ADHD-MA) in Pennsylvania-located elementary schools over a three-year period.

Methods. An ecological study design involving records of 168,825 children from elementary schools in 49 Pennsylvania counties was used. The number of children with ADHD-MA was extracted from an online software specifically designed for allowing nurses to record health conditions in schools. Daily measurements of air pollutants were gained from the U.S Environmental Protection Agency.

Results. The mean number of ADHD-MA significantly increased over the 3-year period [163.9 (± 70.1) in 2008, 317.2 (± 84.4) in 2009, and 427 (± 101.4) in 2010]. The difference in the number of ADHD-MA among the three years and among the four seasons, for all years, were statistically significant ($P<0.001$). Three air pollutants (SO_2, CO, and $PM_{2.5}$) were significantly associated with ADHD-MA; no interactions among air pollutants were significant.

Conclusion. Air pollution is likely associated with both ADHD incidence and ADHD-MA. Prospective epidemiological and biomedical studies could examine the relationship between air pollution and ADHD symptoms.

What is already known about the topic?

1. Air pollution has severe health effects on populations and children could be the most vulnerable.
2. School administrations are responsible to monitor and inform about the health conditions of their students.

What does this study add?

1. There is a probable link between upper air pollutants and increased intake of ADHD medications.

2. School administrations should closely watch levels of air pollution in their area and inform parents of students with pre-existing conditions about the potentiality of adverse effects imposed on their children.

Keywords: Air pollutants; Attention Deficit Hyperactivity Disorder; Schools; Association.

Introduction

Attention Deficit Disorder with Hyperactivity, also known as Attention Deficit Hyperactivity Disorder (ADHD), is a developmental, neuropsychiatric manifestation of inattention, hyperactivity, and impulsivity presenting in most affected children.[1] ADHD is the most commonly diagnosed neurobehavioral childhood disorder, because its prevalence reaches 8-12% worldwide.[2] In the U.S., 9.4% (6.1 million) children of age 2-17 years had ever diagnosed with ADHD, while 89.4% of them (5.4 million) currently had ADHD. Furthermore, 62.0% of children with current ADHD were taking ADHD medication and 46.7% had received behavioral treatment; 23.0% had not received any treatment. Put differently, 5.2% of U.S. children were taking ADHD medication.[3]

Magnitude of symptoms in individuals with ADHD varies substantially, ranging from mild to severe. Despite this variation, diagnosis relies primarily on child's inability to focus plus activity level.[4] A definitive ADHD diagnosis is only confirmed when primary symptoms are persistent and/or accompanied by additional symptoms.[5] Persistence of ADHD into adolescence and adulthood is not uncommon.[4] Altered behavior of children with ADHD distinguishes them from normal, similar-aged children. Those with ADHD tend to: distract easily; move continuously; dream during the day; not accomplish tasks at school or in the community; and have lower educational achievement. When older, they may engage in risky behaviors, including substance abuse and delinquency. Moreover, other conditions such as conduct disorder, anxiety, depression, oppositional defiant disorder, and obsessive disorder can accompany ADHD.[1,5-7]

ADHD is believed to have hereditary origins; however, numerous studies identified several environmental variables as risk factors or contributors,[8] including food additives, lead contamination,

cigarette and alcohol exposure, and maternal smoking during pregnancy.[9] Another important environmental risk factor hypothesized and explored in several recent studies is air pollution. Due to increasing human activity, enormous amounts of pollutants have been emitted into the atmosphere with industrial discharges and automobile emissions constituting main sources. Indoor air can also be polluted from sources such as second-hand smoke, mold, and cleaning product vapors. Air pollution exposure is linked to many childhood health problems including neurodevelopmental effects. For example, cognitive functions were adversely affected among New York City children prenatally exposed to Polycyclic Aromatic Hydrocarbons (PAH). These children exhibited lower IQ scores at age 5 as compared to children with lower levels of PAH exposure.[10] Investigations of the same children through age 8 identified additional neurobehavioral changes--higher levels of anxiety and depression at 4.8 years of the study and higher levels of attention problems at 4.8 and 7 years.[11]

Furthermore, several studies found an association between ADHD in children and air pollution from outdoor sources, such as traffic air pollution,[12] total polycyclic aromatic hydrocarbons (PAHs), and benzo[a]pyrene (BPA) exposure, and basal ganglia functioning as well as ADHD symptoms in primary school children.[13] Both pre- and postnatal exposure to particulate matter with a diameter of <10 µm (PM_{10}), current exposure to nitrogen dioxide (NO_2), and decreased Normalized Difference Vegetation Index (NDVI) were associated with the higher relative risk of ADHD incidence.[6,14,15]

Two concerns emerged from the limited extant literature regarding effects of air pollution on ADHD among children: 1) the effect of some chemicals present in adulterated air on ADHD incidence has not been investigated and 2) the relationship between air pollution and ADHD symptoms remains largely unexplored. Therefore, the research question of this ecological study was: “Does an association exist between seven selected air pollutants and school-time ADHD medication administration, used as a proxy for ADHD symptoms, among elementary school children.”

Data and Methods

Study population:

For this study, electronic health record (EHR) data from 168,825 students attending elementary schools in 42 of 67 Pennsylvania counties, excluding Philadelphia and surrounding counties, were analyzed. Data were extracted from an EHR imbedded in "Health eTools for Schools" (hereafter called eTools), a web-based information system, used in over 1,100 preK-12 Pennsylvania schools. Annual fluctuations in school involvement created somewhat inconsistent participation rates.[16-18]

Via online access to eTools, school nurses made daily EHR entries for all students who were administered at least one medication. From these entries, daily numbers of students administered an ADHD medication were calculated for every school over three consecutive years, 2008-2010. Incomplete records for which medication entry could not be identified were excluded. ADHD-MA could not be recorded if a child for whom ADHD medications were prescribed was absent from school on a given day or medication was accessed outside of school. Similarly, children with undiagnosed ADHA or a misdiagnosis, and who therefore were not prescribed ADHD medication, were not included in the study population. Records only included student sex and age; race or socioeconomic status data were unavailable at the individual level. Since school attendance is compulsory, Pennsylvania public schools are open to all children regardless of race, ethnicity, family income, sex, or religion, and many parochial schools participated in eTools, data were assumed to be representative of Pennsylvania elementary school students diagnosed with ADHD.

Study Design:

This study used an ecological design, involving cross-sectional daily measurements of seven air pollutants and daily ADHD-MA data from an EHR system. This design provides a gross image of the relationship between variables of interest and responses at a population level, analyzing groups' responses rather than individual responses, thus eliminating inter-individual variability. Analysis of variables and responses at a group level reflect the association of two or more factors related to a

population living in a geographical area. Ecological relations are global indicators usually used to establish hypotheses for causality to be tested by further research. Initial assumptions derived from ecological studies are further tested through additional cohort epidemiological and biomedical studies. Follow-up investigation helps revise hypotheses from previous studies. Group level analysis should be representative for the whole population; in this case, elementary school children living within a state. Almost 170,000 elementary students with EHR lived within the Commonwealth of Pennsylvania.

Data Collection:

As previously indicated, data from daily EHR entries by school nurses were accessed and summed to establish the total daily number of children receiving ADHD medication during 2008, 2009, and 2010, excluding school breaks and holidays. Typically, data were unavailable for summer breaks that generally encompassed the first week of June through the third week of August. Data were also not available for four school breaks, i.e., fall, Thanksgiving, winter, and spring.

Records for seven air pollutants, NO_2, NOx, SO_2, CO, O_3, $PM_{2.5}$, and PM_{10} were obtained from the United States Environmental Protection Agency USEPA website.[19] Records originated from 48 EPA monitoring stations across Pennsylvania. Daily and hourly readings for all air pollutants were available; however, only data from regular schools' days were analyzed. Additionally, only records spanning 1am – 3pm were included as these covered mornings before school started onward throughout the school day. Data for PM_{10} were unavailable from 1am – 3am, and 1pm – 3 pm. SO_2 and NO_2 units of measurements were parts per billion (ppb), CO, O_3, and NOx were parts per million (ppm), and, for $PM_{2.5}$ and PM_{10}, micrograms per cubic meter (mg/m^{-3}).

Analysis:

Poisson repeated measure procedure was used to analyze three years of exposure for each air pollutant, assuming measures were correlated. In general, regression analysis methods of this type have

long been used to link air pollution and health outcomes because variables such as weather changes, seasonal variations, metrological factors, and other confounders can be accounted for in the analysis.[9,10,20-24] Long-term trends and predicting models can be developed, while controlling for confounders, to estimate the magnitude of effect in the short- and long-term.[20]

Poisson repeated measure analysis uses generalized equation estimate (GEE) for repeated measures. GEE is advantageous for analyzing correlated measures even if normality cannot be assumed; a correct specification of the correlation matrix is not required to have a consistent estimator of the regression parameters. Having the predicted correlation matrix closer to the true correlation is preferred to achieve greater statistical accuracy for regression parameter.[25] For this study, the assumption of normality was accepted for correlations among measures. Repeated measures were taken for the same day over the study period, and each day measure was represented by its mean. One-way ANOVA tested for differences in the number of ADHD medication administrations, as were seasonal differences in ADHD rates. SPSS version 23 was used in the analysis; a p-value of ($p<0.05$) was considered significant.

Ethical Consideration

This study was approved by the Institutional Review Board of Indiana University Bloomington, United States.

Results

EHR entry records indicated equal student distribution by gender, with 75% racially white. Based on school level data regarding percent of students in each school eligible for free or reduced-price lunch and school zip code, one in four students was low SES and most lived in high population density urban and suburban areas (Table 1).[26]

At 42%, ADHD-MA was the most common reason for students to visit the school nurse. Number of visits per month ranged between 121 and 518, whereas the mean of ADHD-MA visits increased from

163.9 (± 70.1) in 2008 to 317.2 (± 84.4) in 2009 and 427 (± 101.4) in 2010 (Figure 1). Apart from summer break months (June-August), ADHD-MA events generally increased from January to December each year. For 2008, 2009, and 2010, the lowest events were observed in January (124), January (281), and February (419), respectively, whereas the highest events were reported in December (276), December (431), and May (519), respectively. Mean differences in ADHD-MA event between years proved significant (P< 0.001), with post-hoc multiple comparison analysis finding a statistically significant difference between following years; 2008 and 2009 (P<0.001), 2008 and 2010 (P<0.001), and 2009 and 2010 (P<0.006). Difference of ADHD-MA visit rates among seasons was also statistically significant (P<0.001); post-hoc multiple comparison analysis found statistically significant differences between all seasons, except for spring and winter. Means by season, excluding summer, for all years revealed that fall as had the highest ADHD-MA rate with 367.81 (±96.783) events, followed by 319.65 (±153.548) in spring, and 297.17 (±144.635) in winter.

Levels of O_3, SO_2, CO, NO_2, NOx, $PM_{2.5}$, and PM_{10}, varied across seasons (Table 2). Summer had the lowest concentrations of SO_2, CO, NO_2, and NOx over the three-years. Air pollutants, except for O_3 and PM_{10}, were highest in winter.

Poisson regression showed significant associations between SO_2, CO, and $PM_{2.5}$ concentrations and ADHD-MA (Table 3). The association was strongest for CO, which was positively associated with ADHD-MA with a factor of 2 [95% CI: .303 – 3.75, p-value=.021], followed by SO_2, which was negatively associated with ADHD-MA [B= -.092, 95% CI: -.160 – -.024, p-value=.008]. $PM_{2.5}$ association was the weakest; a positive factor of .007 [95% CI: .011 – 11.91, p-value=.001]. On the other hand, O_3, PM_{10}, NO_2 and NOx were not statistically significantly associated with ADHD-MA. Further, the Interaction effect among the seven air pollutants was also not statistically significant [B= 7.5835E-10, 95% CI: -5.0063E-9 – 6.523E-9, p-value = .797].

Discussion

Although based on aggregate data, results represented the cyclical changes in ADHD-MA and, most importantly, continuously increasing burden of ADHD-MA on both Pennsylvania elementary school children and school nurse resources. While the 2.5-fold increase in mean ADHD-MA visits from 2008 to 2010 could be due to the same students receiving more frequent doses, the more likely explanation is that the number of students who had ADHD-MA from a school nurse daily increased during the three years period.

Weekly measurements for air pollutants provided a credible prediction for the number of ADHD-MA-related student/school nurse visits. Interestingly, significant predictors of ADHD-MA visits had a positive estimate (B) value, except for SO_2, which indicated an inverse relationship. Therefore, no clear explanation of the link between ADHD-MA with air pollution was found, except for seasonal fluctuations. This is contradictory to a study by Yorifuji et al (2017) that found a positive association of SO_2 with unfavorable behavioral problems related to attention.[27] However, the association reported by Yorifuji was for prenatal rather than postnatal exposures. Moreover, only $PM_{2.5}$, but not PM_{10} was significantly associated with ADHD-MA in the current study. Meantime, the relationship of PM_{10} and ADHD is not consistent across studies. While some studies have found a positive and even strong association of PM_{10} with ADHD,[6,28] other studies concluded insignificant or inconsistent association.[23,29] Nevertheless, air pollutants that were positively associated with ADHD-MA visit rates (i.e. CO and $PM_{2.5}$) are well known for causing adverse health effects, including ADHD.[15,30,31]

Air pollutants used in the model to predict ADHD-MA were similarly used in other studies to predict prevalence or incidence of ADHD.[14,15,32,33] In addition, pollutants that were found significant with ADHD-MA in the current study, were likewise significantly associated with ADHD in other studies. For example, the positive association of ADHD with $PM_{2.5}$ were reported by Newman et al (2013) and Fuertes et al (2016).[12,23] Moreover, a study by Markevych et al. (2018) and another by Min and Min (2017) found that higher levels of NO_2 were associated with higher relative ADHD risk.[14,28] Furthermore, prenatal

exposure to air pollutants, including PM, NO_2 and $SO_{2,}$ during gestation was associated with higher risk for behavioral problems related to attention and delinquent or aggressive behavior in Japanese children.[24] Nevertheless, other studies found no association of ADHD with traffic-related air pollution.[22,29]

Whether the association between air pollution and ADHD is considered valid or not, other factors, such as epigenetics, play a role in ADHD etiology. For instance, interaction of genes with environmental stressors are known to predispose the occurrence of ADHD in children. Studies supported the contention that genetic factors can intervene and moderate the relation between environmental stress and behavioral deficits outcomes.[15,34,35] Other factors related to ADHD include SES and familial environments.[14,15,36-39] Such factors vary among regions and communities in Pennsylvania, making the cause – effect relationship of air pollution with ADHD more complex. Unfortunately, due to the nature of the study design and data availability, neither genetic background, SES nor familial environment could be measured. Nonetheless, the large sample size and the availability of measurements over 3-year period were supportive for a potential relationship between ADHD-MA and air pollution.

If the prevalence of ADHD among the Pennsylvania elementary school children mirrored that of the US, then 8,779 (5.2%) of the 168,825 subjects in this study would have ADHD.[3] Therefore, the clear majority possibly received ADHD-MA outside of school hours. However, the frequency of ADHD-MA does not indicate ADHD diagnosis, which is based on the judgment of a qualified health care specialist and health determinants that influence access to healthcare. Furthermore, ADHD symptoms resemble some other behavioral diseases that are treated with similar medications, including stimulants such as amphetamine and methylphenidate, which are effective for some, but not all, ADHD patients.[40] This further complicates the issue of the types of medications nurses used to manage symptoms, particularly for children who are not responsive for some medications. In addition, the frequent administration of medication for some children is attributed to clinical management strategy, especially when some

children are switched between different medications, such as stimulants and non–stimulants, with adjusted doses based on symptoms, to decide which one at which dose works for the child.[41]

All of this notwithstanding, evidence of environmental influences on ADHD indicates that ADHD may be related to multiple environmental factor including chemical, physical, or social exposures that interact with ADHD-related genes and, thereby, contribute to ADHD incidences. Findings of this study indicate that monitoring of overall air pollution is among the practical tools that can be used for predicting not only ADHD incidence, but also ADHD symptoms. Further prospective studies can help determine the strength of evidence for developing guidelines that recommend school nurses and parents of children with ADHD to take precautions during specific days or periods of the year when higher pollutant concentrations are tending to increase.

Conclusion

ADHD-MA among Pennsylvania elementary school children increased over three years (2008 – 2010), with fall having the highest rate of ADHD-MA. While causal mechanisms are unknown, concentrations of SO_2, CO, and $PM_{2.5}$ were found to be significantly associated ADHD-MA patterns. Nevertheless, this association reveals that ADHD is affected by the proximate environment and/or direct air pollutant exposures. Moreover, monitored and predicted levels of air pollutant concentrations can potentially be used as an indicator of the overall impact of ADHD on school children. Accordingly, preventative initiatives may be developed and implemented to minimize exposures of children with ADHD during days and/or periods of the year when high concentrations of air pollutants are predicted.

Symptomatic management of ADHD, as a highly complex disorder, cannot be easily predicted by a single factor or even multiple factors and their interactions, making development of a comprehensive model that includes all known factors affecting ADHD difficult. Therefore, familial, genetic, and environmental factors known to contribute to ADHD should be comprehensively and simultaneously

examined in future research to obtain reasonable estimates of increases in ADHD symptoms of individuals within defined communities.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Authors Contributions

Rami Saadeh: conceptualization, study design, statistical analysis, manuscript writing.

Wasantha P. Jayawardene: revision and critical editing

David Lohrmann: revision and critical editing

Yousef Agha: data collection and study design.

References

1. Centers for Disease Control and Prevention C. Attention Deficit Hyperactivity Disorder (ADHD). 2014; http://www.cdc.gov/nchs/fastats/adhd.htm.
2. Faraone SV, Mick E. Molecular genetics of attention deficit hyperactivity disorder. Psychiatr Clin North Am. 2010;33(1):159-180.

3. Danielson ML, Bitsko RH, Ghandour RM, Holbrook JR, Kogan MD, Blumberg SJ. Prevalence of Parent-Reported ADHD Diagnosis and Associated Treatment Among U.S. Children and Adolescents, 2016. J Clin Child Adolesc Psychol. 2018;47(2):199-212.
4. Buitelaar J, Medori R. Treating attention-deficit/hyperactivity disorder beyond symptom control alone in children and adolescents: a review of the potential benefits of long-acting stimulants. Eur Child Adolesc Psychiatry. 2010;19(4):325-340.
5. Bush G. Attention-deficit/hyperactivity disorder and attention networks. Neuropsychopharmacology. 2010;35(1):278-300.
6. Siddique S, Banerjee M, Ray MR, Lahiri T. Attention-deficit hyperactivity disorder in children chronically exposed to high level of vehicular pollution. Eur J Pediatr. 2011;170(7):923-929.
7. Chen MH, Su TP, Chen YS, Hsu JW, Huang KL, Chang WH, et al. Attention deficit hyperactivity disorder, tic disorder, and allergy: is there a link? A nationwide population-based study. J Child Psychol Psychiatry. 2013;54(5):545-551.
8. Ballard S, Bolan M, Burton M, Snyder S, Pasterczyk-Seabolt C, Martin D. The neurological basis of attention deficit hyperactivity disorder. Adolescence. 1997;32(128):855-862.
9. Banerjee TD, Middleton F, Faraone SV. Environmental risk factors for attention-deficit hyperactivity disorder. Acta Paediatr. 2007;96(9):1269-1274.
10. Perera FP, Li Z, Whyatt R, Hoepner L, Wang S, Camann D, et al. Prenatal airborne polycyclic aromatic hydrocarbon exposure and child IQ at age 5 years. Pediatrics. 2009;124(2):e195-202.
11. Perera FP, Wang S, Vishnevetsky J, Zhang B, Cole KJ, Tang D, et al. Polycyclic aromatic hydrocarbons-aromatic DNA adducts in cord blood and behavior scores in New York city children. Environ Health Perspect. 2011;119(8):1176-1181.
12. Newman NC, Ryan P, Lemasters G, Levin L, Bernstein D, Hershey GK, et al. Traffic-related air pollution exposure in the first year of life and behavioral scores at 7 years of age. Environ Health Perspect. 2013;121(6):731-736.
13. Mortamais M, Pujol J, van Drooge BL, Macia D, Martinez-Vilavella G, Reynes C, et al. Effect of exposure to polycyclic aromatic hydrocarbons on basal ganglia and attention-deficit hyperactivity disorder symptoms in primary school children. Environ Int. 2017;105:12-19.
14. Markevych I, Tesch F, Datzmann T, Romanos M, Schmitt J, Heinrich J. Outdoor air pollution, greenspace, and incidence of ADHD: A semi-individual study. Sci Total Environ. 2018;642:1362-1368.
15. Myhre O, Lag M, Villanger GD, Oftedal B, Ovrevik J, Holme JA, et al. Early life exposure to air pollution particulate matter (PM) as risk factor for attention deficit/hyperactivity disorder (ADHD): Need for novel strategies for mechanisms and causalities. Toxicol Appl Pharmacol. 2018;354:196-214.
16. YoussefAgha AH, Jayawardene WP, Lohrmann DK, El Afandi GS. Air pollution indicators predict outbreaks of asthma exacerbations among elementary school children: integration of daily environmental and school health surveillance systems in Pennsylvania. J Environ Monit. 2012;14(12):3202-3210.
17. Youssefagha AH, Lohrmann DK, Jayawardene WP, El Afandi GS. Upper-air observation indicators predict outbreaks of asthma exacerbations among elementary school children: integration of daily environmental and school health surveillance systems in Pennsylvania. J Asthma. 2012;49(5):464-473.
18. Jayawardene WP, Youssefagha AH, Lohrmann DK, El Afandi GS. Prediction of asthma exacerbations among children through integrating air pollution, upper atmosphere, and school health surveillances. Allergy Asthma Proc. 2013;34(1):e1-8.
19. Environmental Protection Agency (EPA). Pre-Generated Data Files. 2016; http://aqsdr1.epa.gov/aqsweb/aqstmp/airdata/download_files.html.

20. Smith RL, Davis JM, Sacks J, Speckman P, Styer P. Regression models for air pollution and daily mortality: analysis of data from Birmingham, Alabama. Environmetrics. 2000;11(6):719-743.
21. Froehlich TE, Lanphear BP, Auinger P, Hornung R, Epstein JN, Braun J, et al. Association of tobacco and lead exposures with attention-deficit/hyperactivity disorder. Pediatrics. 2009;124(6):e1054-1063.
22. Forns J, Dadvand P, Foraster M, Alvarez-Pedrerol M, Rivas I, Lopez-Vicente M, et al. Traffic-Related Air Pollution, Noise at School, and Behavioral Problems in Barcelona Schoolchildren: A Cross-Sectional Study. Environ Health Perspect. 2016;124(4):529-535.
23. Fuertes E, Standl M, Forns J, Berdel D, Garcia-Aymerich J, Markevych I, et al. Traffic-related air pollution and hyperactivity/inattention, dyslexia and dyscalculia in adolescents of the German GINIplus and LISAplus birth cohorts. Environ Int. 2016;97:85-92.
24. Yorifuji T, Kashima S, Diez MH, Kado Y, Sanada S, Doi H. Prenatal exposure to outdoor air pollution and child behavioral problems at school age in Japan. Environ Int. 2017;99:192-198.
25. Ballinger GA. Using Generalized Estimating Equations for Longitudinal Data Analysis. Organizational Research Methods. 2004;7(2):127-150.
26. U.S. Department of Education (DoE) IoES, National Center for Education Statistics. Search for Public Schools. 2015; CCD Public school data 2013-2014, 2014-2015 school years. 2013 - 2015 http://nces.ed.gov/ccd/schoolsearch/. Accessed October 29, 2015.
27. Yorifuji T, Kashima S, Diez MH, Kado Y, Sanada S, Doi H. Prenatal exposure to outdoor air pollution and child behavioral problems at school age in Japan. Environment International. 2017;99:192-198.
28. Min JY, Min KB. Exposure to ambient PM10 and NO2 and the incidence of attention-deficit hyperactivity disorder in childhood. Environ Int. 2017;99:221-227.
29. Gong T, Almqvist C, Bolte S, Lichtenstein P, Anckarsater H, Lind T, et al. Exposure to air pollution from traffic and neurodevelopmental disorders in Swedish twins. Twin Res Hum Genet. 2014;17(6):553-562.
30. Environmental Protection Agency (EPA). Carbon Monoxide (CO) Pollution in Outdoor Air. 2016; https://www.epa.gov/co-pollution/basic-information-about-carbon-monoxide-co-outdoor-air-pollution#Effects.
31. Environmental Protection Agency (EPA). Particulate Matter (PM) Pollution. 2016; https://www.epa.gov/pm-pollution/health-and-environmental-effects-particulate-matter-pm.
32. Ha S, Yeung E, Bell E, Insaf T, Ghassabian A, Bell G, et al. Prenatal and early life exposures to ambient air pollution and development. Environmental Research. 2019.
33. Aghaei M, Janjani H, Yousefian F, Jamal A, Yunesian M. Association between ambient gaseous and particulate air pollutants and attention deficit hyperactivity disorder (ADHD) in children; a systematic review. Environ Res. 2019;173:135-156.
34. Rowland AS, Lesesne CA, Abramowitz AJ. The epidemiology of attention-deficit/hyperactivity disorder (ADHD): a public health view. Ment Retard Dev Disabil Res Rev. 2002;8(3):162-170.
35. Kim-Cohen J, Caspi A, Taylor A, Williams B, Newcombe R, Craig IW, et al. MAOA, maltreatment, and gene-environment interaction predicting children's mental health: new evidence and a meta-analysis. Mol Psychiatry. 2006;11(10):903-913.
36. Biederman J, Milberger S, Faraone SV, Guite J, Warburton R. Associations between childhood asthma and ADHD: issues of psychiatric comorbidity and familiality. J Am Acad Child Adolesc Psychiatry. 1994;33(6):842-848.
37. Biederman J, Milberger S, Faraone SV, Kiely K, Guite J, Mick E, et al. Family-environment risk factors for attention-deficit hyperactivity disorder. A test of Rutter's indicators of adversity. Arch Gen Psychiatry. 1995;52(6):464-470.

38. Pressman LJ, Loo SK, Carpenter EM, Asarnow JR, Lynn D, McCracken JT, et al. Relationship of family environment and parental psychiatric diagnosis to impairment in ADHD. J Am Acad Child Adolesc Psychiatry. 2006;45(3):346-354.
39. Schroeder VM, Kelley ML. Associations Between Family Environment, Parenting Practices, and Executive Functioning of Children with and Without ADHD. Child and Family Studies. 2009;10:227-235.
40. Hechtman L. Treatment of ADHD in patients unresponsive to methylphenidate. J Psychiatry Neurosci. 2011;36(3):216.
41. Ben Amor L, Sikirica V, Cloutier M, Lachaine J, Guerin A, Carter V, et al. Combination and switching of stimulants in children and adolescents with attention deficit/hyperactivity disorder in quebec. J Can Acad Child Adolesc Psychiatry. 2014;23(3):157-166.