

Ambient Air Pollution and Diabetes

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ABSTRACT

This review critically evaluates the complex processes and epidemiological data between ambient air pollution and diabetes. Air pollutants such as particulate matter, nitrogen dioxide, and ozone have increased due to urbanization and industrialization. According to new study, chronic exposure to these contaminants increases the incidence of diabetes mellitus. The review synthesizes epidemiological, animal, and mechanistic data to determine how air pollution may cause and advance diabetes. Oxidative damage, inflammation, insulin resistance, and adipose tissue function are examined. The research also highlights how sensitive groups, such as those with pre-existing metabolic disorders, increase diabetes susceptibility in air pollution exposure. The study also discusses the worldwide burden of diabetes and ambient air pollution and the necessity for environmental scientists, epidemiologists, and healthcare professionals to collaborate on mitigation measures and public health initiatives. This comprehensive review seeks to inform policymakers, healthcare professionals, and researchers about the complex interactions that contribute to the growing public health risks of ambient air pollution and diabetes.

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BACKGROUND

Ambient air pollution, an insidious yet ubiquitous presence in our environment, refers to the presence of harmful substances in the air we breathe. These detrimental pollutants, including particulate matter (PM), nitrogen dioxide (NO₂), and ozone (O₃),¹ originate from a multitude of sources, predominantly vehicular emissions, power plants, and industrial activities². The pervasiveness of air pollution has transformed it into a pressing global concern³.

Cardiovascular diseases, cerebral vascular disease, and ischemic heart disease are among the conditions that air pollution may cause or worsen⁴⁻⁸. The neurological system⁹, the digestive system¹⁰, and the urinary system¹¹ are all negatively impacted by air pollution. There was evidence that long-term exposure to ambient air pollution increased the risk of death from any cause¹². Numerous respiratory illnesses, including asthma, chronic obstructive pulmonary disease (COPD), and lung cancer, are caused or made worse by air pollution^{13, 14-17}. A number of chronic illnesses, including diabetes, have been shown to be strongly

associated with exposure to polluted air, making this a major public health concern^{18, 19}.

Diabetes (DM), a metabolic disorder characterized by elevated blood sugar levels, arises from either insufficient insulin production or the body's inability to effectively utilize insulin. Insulin, a crucial hormone, facilitates the body's glucose uptake for energy generation²⁰. The intricate relationship between ambient air pollution and DM has garnered substantial attention due to its profound implications for public health. Delving into this association is of paramount importance, considering the widespread nature of air pollution as an environmental hazard and the escalating prevalence of DM as a global epidemic.

This review delves into the underlying mechanisms fuelling the connection between ambient air pollution and DM, meticulously examines the robust epidemiological

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evidence supporting this association, and explores the potential pathways through which air pollution may contribute to the onset of DM.

1. Ambient Air Pollution

Ambient air pollution, an insidious yet pervasive aspect of our environment, refers to the presence of harmful substances in the air we breathe. These detrimental pollutants, a complex mixture of solid particles and gases, pose a significant threat to public health, with their detrimental effects extending far beyond respiratory ailments to encompass a wide range of physiological systems.

- PM, a ubiquitous component of ambient air pollution, is a heterogeneous mixture of solid particles and liquid droplets suspended in the air²¹. PM can be classified based on its size, with PM 2.5, the finest particles with a diameter of 2.5 micrometers or less, and PM 10, slightly larger particles with a diameter of 10 micrometers or less, being the most commonly studied fractions^{22, 23}. These minuscule particles, capable of penetrating deep into the lungs^{22,23}, have been linked to a myriad of adverse health effects, including respiratory illnesses, cardiovascular diseases, and infant mortality²⁴.
- Emissions of nitrogen oxide from vehicle engines qualify as a traffic-related contaminant^{25, 26}. When breathed in at high enough concentrations, it irritates the respiratory system and causes respiratory illnesses such as coughing, wheezing, dyspnea, bronchospasm, and pulmonary edema. It seems that these negative effects in humans occur at doses over 0.2 ppm, but at concentrations above 2.0 ppm, T-lymphocytes, especially the CD8+ and NK cells responsible for our immunological response, are affected²⁷. It has been shown that chronic lung illness may be caused by long-term exposure to high amounts of NO₂. Smell impairment may occur after prolonged exposure to NO₂²⁷. Irritation of the eyes, throat, and nose are among the symptoms reported^{27,24}, suggesting that the symptoms are not limited to the respiratory system.
- An important portion of the air pollution, especially in cities, is O₃, a smelly gas produced when nitrogen oxides combine with sunlight and volatile organic

molecules²⁸. Because of its irritating properties, O₃ may worsen respiratory illnesses like asthma and bronchitis and irritate the lungs. Furthermore, O₃ exposure may lead to diminished cognitive performance, decreased lung function, and an increased vulnerability to respiratory infections²⁸.

The presence of these harmful substances in the air we breathe highlights the pressing need for effective strategies to mitigate ambient air pollution.

2. Health Effects of Air Pollution

The insidious effects of ambient air pollution extend far beyond DM, encompassing a broad spectrum of adverse health outcomes. Its detrimental impact on respiratory health is well documented, with exposure to air pollutants linked to an increased risk of respiratory infections, asthma, and COPD²⁴.

These far-reaching health consequences underscore the urgent need for comprehensive mitigation strategies to address the multifaceted threat posed by ambient air pollution. In addition to DM, air pollution has been linked to a number of other health problems, including:

Air pollution, a pervasive environmental hazard, extends its detrimental impact on DM²⁹ and encompassing a range of health complications. Its insidious effects manifest in the form of:

1. **Respiratory Problems:** Air pollution triggers respiratory ailments, including asthma and COPD, by inflaming and damaging the airways²⁴.
2. **Cardiovascular Diseases:** Air pollution exacerbates cardiovascular diseases, such as heart attacks and strokes, by promoting atherosclerosis, inflammation, and blood clotting abnormalities³⁰.
3. **Cancer:** Chronic exposure to air pollution increases the risk of developing various types of cancer, including lung cancer, due to its carcinogenic properties²⁴.
4. **Premature Death:** Air pollution contributes to premature mortality by accelerating the progression of chronic diseases and increasing susceptibility to acute respiratory infections³.

The intricate relationship between air pollution and DM is influenced by a complex interplay of factors:

1. **Genetic Susceptibility:** Individuals with genetic predisposition may be more susceptible to the harmful

effects of air pollution³¹.

2. Lifestyle Factors: Lifestyle factors such as smoking, obesity, and physical inactivity amplify the risk of developing DM, further potentiating the adverse effects of air pollution³².

3. Air Pollution and DM

More and more research points to air pollution as a major risk factor for type 2 diabetes (T2D)³³. The link between air pollution and DM has been the subject of many investigations^{33,34}. Epidemiological research and experimental studies offer data confirming the association between exposure to pollutants and increased DM risk^{34,19}. These results stress the need for more studies in this field. The risk of developing gestational DM and of requiring hospitalisation for type 2 diabetes were both linked to prolonged exposure to PM2.5 components, according to studies³⁵⁻³⁷. Although age may moderate the aforementioned associations and organic matter may be the primary mediator of the relationship between PM2.5 and DM, another study found that long-term exposure to PM2.5 (black carbon, nitrate, ammonium, soil particles, and organic matter) is positively associated with DM. This research identifies the factors that contribute to the link between PM2.5 and DM and recommends regulating the production of organic waste in order to reduce the prevalence of PM2.5-related DM³⁸. The positive relationships between PM2.5 and the incidence of T2D mellitus were revealed in the meta-analysis of cohort studies. The results shown that the risk of developing T2D mellitus would rise by 25% in the long-term exposure for every 10- $\mu\text{g}/\text{m}^3$ increase in PM2.5³⁹. In a large Italian population sample, a cross-sectional investigation indicated a statistically significant correlation between self-reported DM mellitus and yearly mean area levels of all air pollutants tested (PM10, PM2.5, NO2, and O3)⁴⁰. Reduced glucose metabolism is one effect of NO2 exposure⁴¹, although increased levels of fasting blood glucose (FBG) and glycated haemoglobin (HbA1c) were seen in PM2.5 exposure^{42,43}. There was a robust correlation between changes in FBG levels and daily exposure to air pollutants, according to Chen et al.⁴⁴. Both FBG and HbA1c levels were shown to be raised after brief exposure to PM10, according to Chuang et al.⁴⁵.

Based on these results, lowering people's exposure to air

pollution should be a top priority in public health initiatives aimed at avoiding type 2 diabetes. There is an immediate need for comprehensive measures to reduce air pollution emissions and defend public health from its negative effects, since more and more studies are connecting it to DM.

3.1 Mechanisms of Impact

While the precise mechanisms underlying this association are still being elucidated, emerging research indicates that air pollution's detrimental effects on insulin sensitivity [46] and inflammation⁴⁷ may play a pivotal role in DM development. Additionally, air pollution can exacerbate the symptoms of individuals already diagnosed with DM, posing further health complications. As we breathe in air laden with pollutants, these harmful substances can infiltrate our bloodstream, triggering a cascade of detrimental effects.

Oxidative stress and inflammation, two key drivers of the diabetic pathology, are activated by air pollutants. Oxidative stress wreaks havoc on cellular functions, ultimately leading to insulin resistance⁴⁸. Furthermore, pollutants disrupt the delicate balance of adipokines, hormones secreted by adipose tissue, further exacerbating metabolic dysfunction.

Researchers have delved into various pathways to elucidate the intricate connection between air pollution, gut microbiota and DM. These proposed mechanisms encompass the impact of pollutants on mitochondrial function, alterations in gut microbiota, and disruptions in circadian rhythms⁴⁹⁻⁵⁶. Exploring these potential pathways provides a more comprehensive understanding of how air pollution may contribute to the onset of DM.

Inflammation, a hallmark of air pollution exposure, sets the stage for cellular and tissue damage, extending to the pancreas⁵⁷. This vital organ plays a crucial role in glucose regulation by producing insulin, a hormone that ensures balanced blood sugar levels⁵⁸. When the pancreas falls victim to air pollution's toxic onslaught, its ability to produce insulin diminishes, paving the way for DM development. One of the primary mechanisms by which air pollution promotes DM development is through the damage it inflicts on the pancreas, the insulin-producing organ. When the pancreas succumbs to this damage, its insulin production capacity dwindles, leading to the development of DM.

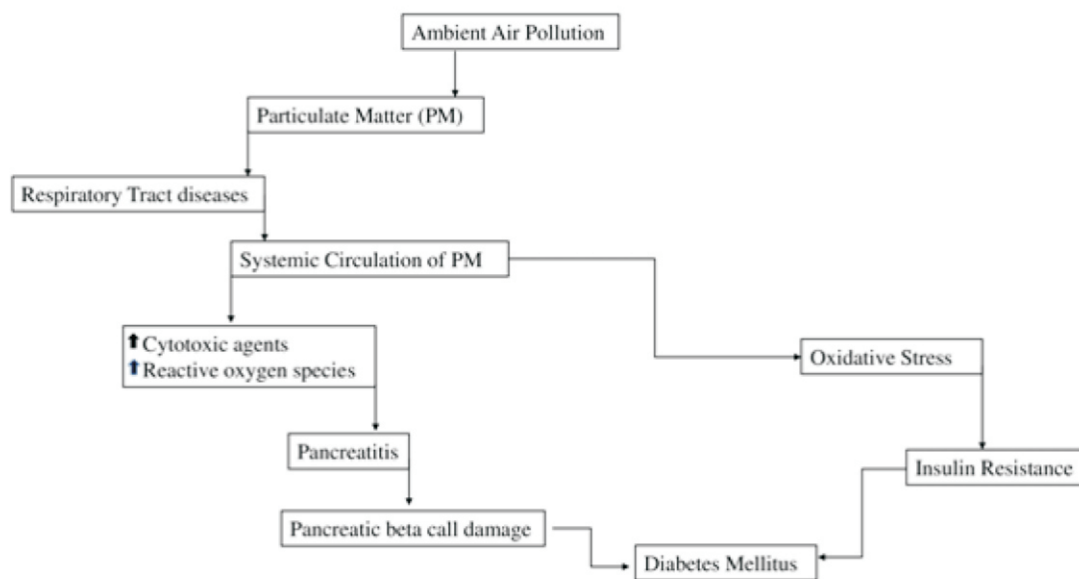


Fig 1. Pictorial mechanism underlying pollution mediated diabetes mellitus

Additionally, air pollution can orchestrate a surge in inflammation throughout the body. While inflammation serves as a natural defence mechanism, its excessive activation can damage cells and tissues. When inflammation takes hold in the pancreas, it disrupts the function of beta cells, the insulin-producing cells. As beta cells falter in their insulin production, the risk of DM escalates.

1. Mitigation Strategies

There are a number of potential strategies that can be used to reduce the impact of air pollution on DM risk. Various mitigation strategies that could be considered include policy interventions, such as stricter emission regulations, promoting clean energy solutions, and fostering public awareness about the health effects of air pollution. Addressing this issue requires a multi-faceted approach.

1. Firstly, we must reduce emissions from vehicles, power plants, and industrial facilities through stricter regulations and the adoption of cleaner technologies.
2. Transitioning to renewable energy sources like solar and wind power is crucial to curb fossil fuel dependence and its associated emissions.
3. Additionally, promoting public transportation, cycling, and walkable infrastructure can significantly reduce reliance on personal vehicles and their harmful emissions.

4. Planting trees serves as a natural air filtration system, effectively removing pollutants and improving air quality.
5. On an individual level, reducing exposure to air pollution is essential.
6. Monitor air quality forecasts and avoid outdoor activities during periods of high pollution.
7. Wearing a mask outdoors, particularly in polluted areas, provides a protective barrier against airborne particles.
8. Keeping windows closed when air quality is poor minimizes indoor pollutant infiltration. Installing air purifiers can further enhance indoor air quality.

By implementing these measures, we can collectively mitigate the adverse effects of ambient air pollution and safeguard public health.

CONCLUSION

In conclusion, the accumulating evidence highlights the intricate interplay between air pollution and DM. The mechanisms by which air pollutants exert their detrimental effects on metabolic health are multifaceted and complex. As our understanding deepens, it becomes increasingly clear that addressing air pollution is not only crucial for respiratory health but also holds significant implications for preventing and managing DM.

DM has reached alarming levels globally. According to recent statistics, the prevalence of DM has been steadily increasing, affecting millions of people worldwide. This rise in cases emphasizes the urgency of understanding the factors contributing to this disease. The evidence linking ambient air pollution and DM is compelling. Understanding the mechanisms involved and implementing effective mitigation strategies is crucial for public health. By addressing air pollution, we have the opportunity to combat not only DM but also other related health conditions. It is imperative to prioritize this issue and work towards a cleaner and healthier environment.

REFERENCES

1. Cao L, Wang L, Wu L, Wang T, Cui X, Yu L et al. Particulate matter and hypertensive disorders in pregnancy: systematic review and meta-analysis. *Public Health*. 2021;200:22-32. doi: 10.1016/j.puhe.2021.08.013, PMID 34653738.
2. World health organization (WHO). Ambient (outdoor) air pollution. Available from: [https://www.who.int/news-room/fact-sheets/detail/ambient-\(outdoor\)-air-quality-and-health](https://www.who.int/news-room/fact-sheets/detail/ambient-(outdoor)-air-quality-and-health).
3. Jiang XQ, Mei XD, Feng D. Air pollution and chronic airway diseases: what should people know and do? *J Thorac Dis*. 2016;8(1):E31-40. doi: 10.3978/j.issn.2072-1439.2015.11.50, PMID 26904251.
4. Watson KE. Air pollution and heart disease. *Rev Cardiovasc Med*. 2006;7(1):44. PMID 16534496.
5. Scarborough P, Allender S, Rayner M, Goldacre M. Contribution of climate and air pollution to variation in coronary heart disease mortality rates in England. *PLOS ONE*. 2012;7(3):e32787. doi: 10.1371/journal.pone.0032787, PMID 22427884.
6. Rückerl R, Ibalá-Mulli A, Koenig W, Schneider A, Woelke G, Cyrys J, et al. Air pollution and markers of inflammation and coagulation in patients with coronary heart disease. *Am J Respir Crit Care Med*. 2006;173(4):432-41. doi: 10.1164/rccm.200507-1123OC, PMID 16293802.
7. Hassing C, Twickler M, Brunekreef B, Cassee F, Doevendans P, Kastelein J, et al. Particulate air pollution, coronary heart disease and individual risk assessment: a general overview. *Eur J Cardiovasc Prev Rehabil*. 2009;16(1):10-5. doi: 10.1097/HJR.0b013e32831de25d, PMID 19165090.
8. Gold DR, Samet JM. Air pollution, climate, and heart disease. *Circulation*. 2013;128(21):e411-4. doi: 10.1161/CIRCULATIONAHA.113.003988, PMID 24249623.
9. Genc S, Zadeoglulari Z, Fuss SH, Genc K. The adverse effects of air pollution on the nervous system. *J Toxicol*. 2012;2012:782462. doi: 10.1155/2012/782462, PMID 22523490.
10. Kaplan GG, Tanyingoh D, Dixon E, Johnson M, Wheeler AJ, Myers RP, et al. Ambient ozone concentrations and the risk of perforated and nonperforated appendicitis: a multicity case-crossover study. *Environ Health Perspect*. 2013;121(8):939-43. doi: 10.1289/ehp.1206085, PMID 23842601.
11. Castaño-Vinyals G, Cantor KP, Malats N, Tardon A, Garcia-Closas R, Serra C, et al. Air pollution and risk of urinary bladder cancer in a case-control study in Spain. *Occup Environ Med*. 2008;65(1):56-60. doi: 10.1136/oem.2007.034348, PMID 17634245.
12. Carey IM, Atkinson RW, Kent AJ, van Staa T, Cook DG, Anderson HR. Mortality associations with long-term exposure to outdoor air pollution in a national English cohort. *Am J Respir Crit Care Med*. 2013;187(11):1226-33. doi: 10.1164/rccm.201210-1758OC, PMID 23590261.
13. Faustini A, Stafoggia M, Colais P, Berti G, Bisanti L, Cadum E, et al. Air pollution and multiple acute respiratory outcomes. *Eur Respir J*. 2013;42(2):304-13. doi: 10.1183/09031936.00128712, PMID 23314899.
14. Kelly FJ, Fussell JC. Air pollution and airway disease. *Clin Exp Allergy*. 2011;41(8):1059-71. doi: 10.1111/j.1365-2222.2011.03776.x, PMID 21623970.
15. Karakatsani A, Analitis A, Perifanou D, Ayres JG, Harrison RM, Kotronarou A, et al. Particulate matter air pollution and respiratory symptoms in individuals having either asthma or chronic obstructive pulmonary disease: a European multicentre panel study. *Environ*

- Health. 2012;11:75. doi: 10.1186/1476-069X-11-75, PMID 23039312.
16. Vineis P, Hoek G, Krzyzanowski M, Vigna-Taglianti F, Veglia F, Airolidi L, et al. Air pollution and risk of lung cancer in a prospective study in Europe. *Int J Cancer*. 2006;119(1):169-74. doi: 10.1002/ijc.21801, PMID 16463382.
17. Sax SN, Zu K, Goodman JE. Air pollution and lung cancer in Europe. *Lancet Oncol*. 2013;14(11):e439-40. doi: 10.1016/S1470-2045(13)70438-8, PMID 24079870.
18. Eze IC, Hemkens LG, Bucher HC, Hoffmann B, Schindler C, Künzli N et al. Association between ambient air pollution and diabetes mellitus in Europe and North America: systematic review and meta-analysis. *Environ Health Perspect*. 2015;123(5):381-9. doi: 10.1289/ehp.1307823, PMID 25625876.
19. Yang BY, Fan S, Thiering E, Seissler J, Nowak D, Dong GH et al. Ambient air pollution and diabetes: A systematic review and meta-analysis. *Environ Res*. 2020;200:108817. doi: 10.1016/j.envres.2019.108817, PMID 31627156.
20. Galicia-Garcia U, Benito-Vicente A, Jebbari S, Larrea-Sebal A, Siddiqi H, Uribe KB et al. Pathophysiology of type 2 diabetes mellitus. *Int J Mol Sci*. 2020;21(17):6275. doi: 10.3390/ijms21176275, PMID 32872570.
21. Cheung K, Daher N, Kam W, Shafer MM, Ning Z, Schauer JJ, et al. Spatial and temporal variation of chemical composition and mass closure of ambient coarse particulate matter (PM_{10/2.5}) in the Los Angeles area. *Atmos Environ*. 2011;45(16):2651-62. doi: 10.1016/j.atmosenv.2011.02.066.
22. Kelishadi R, Poursafa P. Air pollution and non-respiratory health hazards for children. *Arch Med Sci*. 2010;6(4):483-95. doi: 10.5114/aoms.2010.14458, PMID 22371790.
23. Zhang L, Yang Y, Li Y, Qian ZM, Xiao W, Wang X, et al. Short-term and long-term effects of PM_{2.5} on acute nasopharyngitis in 10 communities of Guangdong, China. *Sci Total Environ*. 2019;688:136-42. doi: 10.1016/j.scitotenv.2019.05.470, PMID 31229811.
24. Manisalidis I, Stavropoulou E, Stavropoulos A, Bezirtzoglou E. Environmental and health impacts of air pollution: a review. *Front Public Health*. 2020;8:14. doi: 10.3389/fpubh.2020.00014, PMID 32154200.
25. Richmond-Bryant J, Owen RC, Graham S, Snyder M, McDow S, Oakes M, et al. Estimation of on-road NO₂ concentrations. *Air Qual Atmos Health*. 2017;10(5):611-25. doi: 10.1007/s11869-016-0455-7, PMID 30245748.
26. Hesterberg TW, Bunn WB, McClellan RO, Hamade AK, Long CM, Valberg PA. Critical review of the human data on short-term nitrogen dioxide (NO₂) exposures: evidence for NO₂ no-effect levels. *Crit Rev Toxicol*. 2009;39(9):743-81. doi: 10.3109/10408440903294945, PMID 19852560.
27. Chen TM, Gokhale J, Shofer S, Kuschner WG. Outdoor air pollution: nitrogen dioxide, sulfur dioxide, and carbon monoxide health effects. *Am J Med Sci*. 2007;333(4):249-56. doi: 10.1097/MAJ.0b013e31803b900f, PMID 17435420.
28. Zhang JJ, Wei Y, Fang Z. Ozone pollution: A major health hazard worldwide. *Front Immunol*. 2019;10:2518. doi: 10.3389/fimmu.2019.02518, PMID 31736954.
29. Eze IC, Schaffner E, Fischer E, Schikowski T, Adam M, Imboden M, et al. Long-term air pollution exposure and diabetes in a population-based Swiss cohort. *Environ Int*. 2014;70:95-105. doi: 10.1016/j.envint.2014.05.014, PMID 24912113.
30. Lee BJ, Kim B, Lee K. Air pollution exposure and cardiovascular disease. *Toxicol Res*. 2014;30(2):71-5. doi: 10.5487/TR.2014.30.2.071, PMID 25071915.
31. Kodavanti UP. Susceptibility variations in air pollution health effects: incorporating neuroendocrine activation. *Toxicol Pathol*. 2019;47(8):962-75. doi: 10.1177/0192623319878402, PMID 31594484.
32. Niemann B, Rohrbach S, Miller MR, Newby DE, Fuster V, Kovacic JC. Oxidative stress and cardiovascular risk: obesity, diabetes, smoking, and pollution: Part 3 of a 3-Part Series. *J Am Coll Cardiol*. 2017;70(2):230-51. doi: 10.1016/j.jacc.2017.05.043, PMID 28683970.
33. Wu Y, Zhang S, Qian SE, Cai M, Li H, Wang C et al. Ambient air pollution associated with incidence and dynamic progression of type 2 diabetes: a trajectory

- analysis of a population-based cohort. *BMC Med.* 2022;20(1):375. doi: 10.1186/s12916-022-02573-0, PMID 36310158.
34. Eze IC, Hemkens LG, Bucher HC, Hoffmann B, Schindler C, Künzli N et al. Association between ambient air pollution and diabetes mellitus in Europe and North America: systematic review and meta-analysis. *Environ Health Perspect.* 2015;123(5):381-9. doi: 10.1289/ehp.1307823, PMID 25625876.
35. Sun S, Qiu H, Ho KF, Tian L. Chemical components of respirable particulate matter associated with emergency hospital admissions for type 2 diabetes mellitus in Hong Kong. *Environ Int.* 2016;97:93-9. doi: 10.1016/j.envint.2016.10.022, PMID 27835752.
36. Sun Y, Li X, Benmarhnia T, Chen JC, Avila C, Sacks DA et al. Exposure to air pollutant mixture and gestational diabetes mellitus in Southern California: results from electronic health record data of a large pregnancy cohort. *Environ Int.* 2022;158:106888. doi: 10.1016/j.envint.2021.106888, PMID 34563749.
37. Yu G, Ao J, Cai J, Luo Z, Martin R, Donkelaar AV et al. Fine particular matter and its constituents in air pollution and gestational diabetes mellitus. *Environ Int.* 2020;142:105880. doi: 10.1016/j.envint.2020.105880, PMID 32593838.
38. Li S, Guo B, Jiang Y, Wang X, Chen L, Wang X et al. Long-term exposure to ambient PM_{2.5} and its components associated with diabetes: evidence from a large population-based cohort from China. *Diabetes Care.* 2023;46(1):111-9. doi: 10.2337/dc22-1585, PMID 36383478.
39. He D, Wu S, Zhao H, Qiu H, Fu Y, Li X et al. Association between particulate matter 2.5 and diabetes mellitus: A meta-analysis of cohort studies. *J Diabetes Investig.* 2017;8(5):687-96. doi: 10.1111/jdi.12631, PMID 28122165.
40. Orioli R, Cremona G, Ciancarella L, Solimini AG. Association between PM₁₀, PM_{2.5}, NO₂, O₃ and self-reported diabetes in Italy: a cross-sectional, ecological study. *PLOS ONE*(1). 2018;13(1):e0191112. doi: 10.1371/journal.pone.0191112, PMID 29342195.
41. Teichert T, Vossoughi M, Vierkötter A, Sugiri D, Schikowski T, Schulte T et al. Association between traffic-related air pollution, subclinical inflammation and impaired glucose metabolism: results from the SALIA study. *PLOS ONE.* 2013;8(12):e83042. doi: 10.1371/journal.pone.0083042, PMID 24340078.
42. Liu C, Yang C, Zhao Y, Ma Z, Bi J, Liu Y et al. Associations between long-term exposure to ambient particulate air pollution and type 2 diabetes prevalence, blood glucose and glycosylated hemoglobin levels in China. *Environ Int.* 2016;92-93:416-21. doi: 10.1016/j.envint.2016.03.028, PMID 27148900.
43. Peng C, Bind MC, Colicino E, Kloog I, Byun HM, Cantone L et al. Particulate air pollution and fasting blood glucose in nondiabetic individuals: associations and epigenetic mediation in the normative aging study, 2000-2011. *Environ Health Perspect.* 2016;124(11):1715-21. doi: 10.1289/EHP183, PMID 27219535.
44. Chen L, Zhou Y, Li S, Williams G, Kan H, Marks GB et al. Air pollution and fasting blood glucose: A longitudinal study in China. *Sci Total Environ.* 2016;541:750-5. doi: 10.1016/j.scitotenv.2015.09.132, PMID 26433332.
45. Chuang KJ, Yan YH, Cheng TJ. Effect of air pollution on blood pressure, blood lipids, and blood sugar: a population-based approach. *J Occup Environ Med.* 2010;52(3):258-62. doi: 10.1097/JOM.0b013e3181ceff7a, PMID 20190657.
46. Kim JH, Hong YC. GSTM1, GSTT1, and GSTP1 polymorphisms and associations between air pollutants and markers of insulin resistance in elderly Koreans. *Environ Health Perspect.* 2012;120(10):1378-84. doi: 10.1289/ehp.1104406, PMID 22732554.
47. O'Neill MS, Veves A, Sarnat JA, Zanobetti A, Gold DR, Economides PA et al. Air pollution and inflammation in type 2 diabetes: a mechanism for susceptibility. *Occup Environ Med.* 2007;64(6):373-9. doi: 10.1136/oem.2006.030023, PMID 17182639.
48. Haberzettl P, O'Toole TE, Bhatnagar A, Conklin DJ. Exposure to fine particulate air pollution causes vascular insulin resistance by inducing pulmonary oxidative stress. *Environ Health Perspect.*

- 2016;124(12):1830-9. doi: 10.1289/EHP212, PMID 27128347.
49. Kassotis CD, Stapleton HM. Endocrine-mediated mechanisms of metabolic disruption and new approaches to examine the public health threat. *Front Endocrinol.* 2019;10:39. doi: 10.3389/fendo.2019.00039, PMID 30792693.
50. Labaronne E, Pinteaur C, Vega N, Pesenti S, Julien B, Meugnier-Fouilloux E et al. Low-dose pollutant mixture triggers metabolic disturbances in female mice leading to common and specific features as compared to a high-fat diet. *J Nutr Biochem.* 2017;45:83-93. doi: 10.1016/j.jnutbio.2017.04.001, PMID 28433925.
51. Kopp R, Martínez IO, Legradi J, Legler J. Exposure to endocrine disrupting chemicals perturbs lipid metabolism and circadian rhythms. *J Environ Sci (China)*. 2017;62:133-7. doi: 10.1016/j.jes.2017.10.013, PMID 29289284.
52. Egusquiza RJ, Blumberg B. Environmental obesogens and their impact on susceptibility to obesity: new mechanisms and chemicals. *Endocrinology.* 2020;161(3):bqaa024. doi: 10.1210/endo/bqaa024, PMID 32067051.
53. Collins SL, Patterson AD. The gut microbiome: an orchestrator of xenobiotic metabolism. *Acta Pharm Sin B*. 2020;10(1):19-32. doi: 10.1016/j.apsb.2019.12.001, PMID 31998605.
54. Liang Y, Liu D, Zhan J, Luo M, Han J, Wang P et al. New insight into the mechanism of POP-induced obesity: evidence from DDE-altered microbiota. *Chemosphere.* 2020;244:125123. doi: 10.1016/j.chemosphere.2019.125123, PMID 32050320.
55. Claus SP, Guillou H, Ellero-Simatos S. The gut microbiota: a major player in the toxicity of environmental pollutants? *npj Biofilms Microbiomes.* 2016;2:16003. doi: 10.1038/npjbiofilms.2016.3, PMID 28721242.
56. Kish L, Hotte N, Kaplan GG, Vincent R, Tso R, Gänzle M et al. Environmental particulate matter induces murine intestinal inflammatory responses and alters the gut microbiome. *PLOS ONE.* 2013;8(4):e62220. doi: 10.1371/journal.pone.0062220, PMID 23638009.
57. Zorena K, Jaskulak M, Michalska M, Mrugacz M, Vandenbulcke F. Air pollution, oxidative stress, and the risk of development of Type 1 diabetes. *Antioxidants (Basel, Switzerland).* 2022;11(10):1908. doi: 10.3390/antiox11101908, PMID 36290631.
58. Bartolomé A. The pancreatic beta Cell: Editorial [editorial]. *Biomolecules.* 2023;13(3):495. doi: 10.3390/biom13030495, PMID 36979430.