



Air Pollution, Oxidative Stress, and Diabetes: a Life Course Epidemiologic Perspective

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Abstract

Purpose of Review Ambient air pollution is strongly linked to cardiovascular and respiratory diseases. We summarize available published evidence regarding similar associations with diabetes across the life course.

Recent Findings We performed a life-course survey of the recent literature, including prenatal, gestational, childhood/adolescence, and adult exposures to air pollution. Oxidative stress is identified as a key factor in both metabolic dysfunction and the effects of air pollution exposure, especially from fossil fuel combustion products, providing a plausible mechanism for air pollution-diabetes associations. The global burden of diabetes attributed to air pollution exposure is substantial, with a recent estimate that ambient fine particulate matter (PM_{2.5}) exposure contributes to more than 200,000 deaths from diabetes annually.

Summary There is a growing body of literature linking air pollution exposure during childhood and adulthood with diabetes etiology and related cardiometabolic biomarkers. A small number of studies found that exposure to air pollution during pregnancy is associated with elevated gestational diabetes risk among mothers. Studies examining prenatal air pollution exposure and diabetes risk among the offspring, as well as potential transgenerational effects of air pollution exposure, are very limited thus far. This review provides insight into how air pollutants affect diabetes and other metabolic dysfunction-related diseases across the different life stages.

Keywords Air pollution · Diabetes · Particulate matter · Oxidative stress

Introduction

The global prevalence of metabolic syndrome disorders, including diabetes mellitus (DM), has increased over time due to aging populations, growing levels of urbanization, and increasing intake of obesogenic diets. The diabetes epidemic is one of the greatest challenges faced by the world's health care systems [1]. Type 2 diabetes (T2DM) is characterized by high levels of circulating glucose and overall insulin resistance, which relates to the development of vascular and metabolic

dysfunctions [2]. Increased oxidative stress has a central role in metabolic syndrome and its component pathologies, and may be a shared underlying actor in their progressions [3]. There is an emerging body of literature implicating ambient air pollution exposure as a potential risk factor for diabetes, as demonstrated by several literature reviews and meta-analyses [4, 5]. The global disease burden of diabetes attributed to air pollution exposure is substantial, with a recent study estimating that ambient fine particulate matter (PM_{2.5}) contributes to 3.2 million incident cases of diabetes and more than 200,000 deaths from diabetes annually [6•]. Although the majority of the current evidence is based on studies of adults, recent results suggest that air pollution can adversely affect cardiometabolic health and elevate diabetes risk earlier in life, beginning with in utero exposures. Here, we review, summarize, and synthesize recent findings (from 2015 forward) on potential health effects of exposure to air pollution on diabetes risk during different stages of the life course: prenatal, gestational, childhood/adolescence, and adulthood. We also discuss the oxidative stress mechanism potentially underlying these associations.

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Air Pollution and Exposure Assessment

Studies included in this literature review analyzed multiple air pollutants and their associations with diabetes risk. PM_{2.5} refers to fine particulate matter, with aerodynamic diameter of less than 2.5 µm, which can penetrate deep into the lungs. PM_{2.5} composition and toxicity can vary depending on its source. NO_x refers to nitrogen oxides, which are byproducts of high-temperature combustion process, and is a marker of traffic-related air pollution. BC is black carbon, a component of particulate matter formed during diesel fuel combustion, and is another marker of traffic, but one more specific to diesel traffic. Ground-level ozone (O₃) forms when NO₂ and volatile organic compounds react with sunlight and heat. SO₂ is sulfur dioxide, which is formed as a byproduct of fossil fuel combustion mainly from industrial sources. Air pollution exposure assessment is traditionally done via linking measurements from nearby stationary-site monitors to study participants, often at their location of residence. To improve exposure estimates, most recent studies rely on statistical models based on land use information and data from monitoring networks, chemical transport models, and remote sensing data from satellites. Personal-level monitoring, where study participants each carry a portable instrument, is another potential approach, although such applications are usually not feasible due to prohibitive costs.

Epidemiological Studies of Air Pollution's Effects on Diabetes

In this review, we performed a comprehensive survey of the literature published since 2015. We selected this date as it is after a recent meta-analysis [5], and since the majority of the studies has been generated thereafter. We searched the PubMed database for articles that contained the terms in the title and/or abstract that were relevant to the current review. The search terms included air pollution AND (diabetes or diabetes mellitus or gestational diabetes). This resulted in 408 articles that were individually evaluated for their relevance; of these, we included 43 studies that included both relevant exposure information and health endpoints and organized them into different life stages. We also added and described studies analyzing cardiometabolic risk factors (e.g., obesity) when the evidence is limited for a life stage. We summarize our findings in Table 1, and the individual papers are listed and described in Appendix Table 2.

Prenatal Exposure

Prenatal exposure to air pollution could adversely affect cardiometabolic health. As the prenatal period is a

critical period for cardiovascular growth and development, fetuses may be especially vulnerable to the adverse health effects of ambient air pollution. Although numerous studies have demonstrated that air pollution exposure during this period can have transgenerational effects on offspring health outcomes (e.g., higher risk of low birthweight and birth defects), evidence linking prenatal exposure to air pollutants and increased risk of diabetes among offspring is very limited. A single study in Sweden found that maternal exposures to NO_x during third trimester pregnancy and to O₃ during second trimester were associated with offspring risk of developing type 1 diabetes (T1D), after controlling for genetic predisposition of disease [7•]. Exposure to particulate matter (PM) air pollution, but not NO₂, during pregnancy was associated with increased levels of cord plasma insulin at birth among 590 newborns in Belgium, suggesting that prenatal exposure could increase the risk of cardiometabolic dysfunction later in life [8].

Recent studies have also linked in utero exposure with diabetes risk factors such as obesity and high blood pressure, suggesting that exposure during this critical period could contribute to the underlying pathophysiology of diabetes. Prenatal exposure could potentially influence body weight and BMI trajectory, as demonstrated by an analysis of the Children's Health Study finding that near-road freeway NO_x exposure during pregnancy was associated with increased rate of change of childhood BMI and higher attained BMI at age 10, independent of later childhood exposures [9]. The Project Viva cohort in Boston, a prospective cohort of prenatal exposures, pregnancy outcomes, and offspring health exposed to low levels of air pollution, offers detailed insights regarding the potential pathways by which prenatal air pollution exposure could induce adverse cardiometabolic outcomes among the offspring. Among infants exposed to higher traffic-related pollution during the third trimester in this cohort, fetal growth was inhibited while rapid postnatal weight gain was observed [10]. Children whose mothers lived close to a major roadway at the time of pregnancy also had higher markers of cardiovascular risk in early and mid-childhood, including higher BMI, larger waist circumference, and higher leptin concentration [11]. However, the investigators did not find evidence for an effect of prenatal exposure to traffic pollution on BMI trajectory from birth through mid-childhood [12].

Prenatal exposure to air pollution is also linked with elevated blood pressure among the offspring [13–15]. These studies found significant associations between air pollution exposure and elevated offspring blood pressure during the third trimester exposure, but not first or second trimesters, suggesting that this may be the most etiologically relevant

Table 1 Summary of evidence for the association between air pollution and diabetes risk across the life-course

Life-stage	# of studies evaluated	Summary
Prenatal	2, and additional 7 studies on cardiometabolic risk factors	Evidence examining air pollution exposure during pregnancy and diabetes risk among offspring is limited to only two studies that examined T1D risk and cord plasma insulin levels. Multiple studies have evaluated and found associations between prenatal air pollution exposure and cardiometabolic risk factors among offspring, suggesting that transgenerational effects on diabetes risk is plausible.
Gestational	6	There is limited but an emerging body of evidence suggesting that air pollution exposure during pregnancy could lead to gestational diabetes. Additional confirmatory studies are still needed, especially to ascertain the etiologically relevant window of exposure prior to and during pregnancy.
Children/adolescents	7, and additional 3 studies on cardiometabolic risk factors	There is growing evidence linking air pollution exposure with metabolic dysfunction among children and adolescents. Other studies also observed significant associations between air pollution and cardiometabolic risk factors.
Adults	28	The evidence regarding air pollution exposure and diabetes prevalence, incidence, and mortality is generally positive. Several studies also examined the effects of co-exposures, such as noise, with mixed findings. Multiple studies have also evaluated cardiometabolic biomarkers related to diabetes risk. Many of the newer studies were conducted in Asia, but evidence from other regions of the world remains very limited.

time window. Epidemiological studies examining whether prenatal exposures to air pollutants could confer elevated diabetes risk later in life and during adulthood among offspring have not been carried out to date and remains a topic of future research.

Gestational Diabetes

Pregnancy is an especially vulnerable period for development of abnormal glycemia because insulin resistance increases as part of adaption to ensure adequate supply of nutrients to the fetus [16]. Gestational diabetes mellitus (GDM) is defined as glucose intolerance with onset or first recognition in pregnancy, affecting up to 8% of pregnancies in the USA [17]. Women with GDM are more likely to develop preeclampsia and diabetes in the years following pregnancy, and their children are at increased risk of stillbirth, delivery by Cesarean section, macrosomia, overweight, impaired glucose tolerance, and diabetes later in life [18].

Findings from recent studies suggest that exposure to air pollutants during pregnancy may be associated with increased risk of developing GDM. In a study of 410,267 women in Florida, exposures to PM_{2.5} and O₃ during first and second trimesters in single-pollutant models were associated with

increased risk of GDM [19]. Exposure to higher CO, NO, and NO_x levels during pregnancy during first trimester and SO₂ and NO during second trimester increased the risk of GDM among 19,606 women in Taiwan [20]. Maternal exposure to NO_x and SO₂ before conception and during first trimester increased GDM risks among mothers in the USA ($n = 219,952$), but a negative association was found for preconception exposure to O₃ [21]. An analysis of 72,745 pregnancies in Denmark found that NO₂ exposure was significantly associated with GDM, although after adjusting for road traffic noise, the associations became non-significant (HR: 1.22; 95% CI = 0.98–1.53) [22]. Exposures to PM_{2.5} during the second trimester and NO₂ during the first trimester were significantly associated with higher risk of GDM among women in New York City, with stronger associations observed in women who were younger, not receiving Medicaid, and overweight [23]. In the aforementioned Project Viva cohort, exposure to PM_{2.5} among women was generally not associated with GDM, although they found evidence of second trimester exposure and GDM among younger women [24]. Overall, the evidence linking air pollution exposure with GDM is generally positive and growing, but additional studies are still needed, especially to ascertain the etiologically relevant window of exposure prior to and during pregnancy.

Children and Adolescents

A number of recent studies, mostly with cross-sectional or observational study designs, have examined and found significant associations between air pollution exposure during childhood and adolescence with diabetes risk. Chronic exposure to PM₁₀, but not NO_x, CO, and O₃, contributed to the incidence rate of type 1 diabetes among children aged between 0 and 14 years old in Southern Italy [25]. A cross-sectional study of 837 children in two German cohorts found that NO₂ and PM_{2.5} exposures were associated with higher HOMA-IR (homeostatic model assessment for insulin resistance), which remained after adjusting for greenspace [26]. Another cross-sectional study found that among 429 overweight and obese African-American and Latino youth in urban Los Angeles, elevated exposure to PM_{2.5} and NO₂ was associated with a metabolic profile characteristic of increased risk for type 2 diabetes, such as higher fasting insulin, lower insulin sensitivity, higher acute insulin response to glucose, and higher fasting glucose [27]. High exposure to the traffic-related air pollutants PM₁₀, NO₂, and potentially PM_{2.5} accelerated the manifestation of T1D, but only in very young children, independent of levels of urbanization [28]. However, a study of 6807 participants aged 0 to 19 years old at diagnosis in Germany did not find such an association between exposure to air pollutants and acceleration of manifestation of type 1 diabetes [29]. An analysis of 37,372 individuals with type 1 diabetes aged < 21 years in a cross-sectional study also observed negative findings, with accumulated exposure to ozone associated with lower HbA1c and no significant associations observed with PM₁₀ and NO₂ [30].

Longitudinal investigations in children have been limited to a recent study of 314 overweight and obese Latino children in Los Angeles [31••], which found that PM_{2.5} and NO₂ exposures were associated with faster decline in insulin sensitivity and lower insulin sensitivity at age 18 years, independent of adiposity. Declines in insulin sensitivity were compensated by increases in insulin secretion, including increased fasting insulin levels and acute insulin response to glucose, and higher levels of exposures were also associated with a higher BMI and body fat at age 18. In addition, NO₂ exposure negatively influenced β -cell function, measured by a faster decline in disposition index (DI) and a lower DI at age 18, suggesting that higher exposures to air pollutants may contribute to development of type 2 diabetes.

Air pollution exposure may also contribute to development of diabetes risk factors in children. In a

longitudinal study of 4550 children living in Southern California, traffic-related air pollution exposure during childhood was positively associated with BMI, suggesting that air pollution exposure could contribute to obesity in children [32]. Another study of 130 children found that same-day exposure to higher concentrations of ultra-fine particles, but not PM_{2.5}, was associated with higher systolic blood pressure in children [33]. Interaction between air pollution exposure and obesity on blood pressure and hypertension was also observed in a study of 9354 Chinese children [34].

Adults

Numerous investigations found significant associations between multiple air pollutants with diabetes prevalence, incidence, and mortality risk [5, 35, 36, 37•, 38–42]. Recent studies of biomarkers have also improved our understanding of the potential pathways underlying air pollution-induced diabetes. For example, among 1023 Mexican Americans, short-term exposure to PM_{2.5} was associated with lower insulin sensitivity and HDL-to-LDL (low density lipoprotein-to-high density lipoprotein) cholesterol ratio, and higher fasting glucose and insulin, HOMA-IR, total cholesterol, and LDL cholesterol, although the study did not find any associations between traffic-related air pollution and metabolic outcomes [43]. Living closer to a major roadway or acute exposure to traffic-related air pollutants was associated with dysregulated glucose homeostasis, but not with adipokines [44]. A study of 4052 participants in persons without diabetes in Germany found that several diabetes-related biomarkers were associated with air pollution, finding that exposures were negatively associated with adiponectin and positively associated with IL-1RA [45]. In another study of 551 nondiabetic participants, PM_{2.5} was associated with higher fasting blood glucose and higher odds of impaired fasting glucose [46]. PM₁₀ and NO₂ were associated with HbA1c, but not prevalent DM, in a cross-sectional study of 2895 participants in Northern France [47]. An analysis of 2944 participants in Germany found that PM₁₀ was associated with higher HOMA-IR, and NO₂ was associated with HOMA-IR, glucose, insulin, and leptin levels, with stronger associations among those with prediabetes [48]. Another analysis of 73,117 participants in Southern Israel found that 3-month average PM₁₀ was associated with elevated serum glucose, HbA1c, low-density lipoprotein, and triglycerides, with elevated associations observed among subjects with diabetes [49].

Notably, many of the newer studies were conducted in Asia, where potential risk factors for diabetes differ and both diabetes prevalence and ambient air pollution levels are substantially higher than Europe and North America, where most of past studies have been conducted. Among longitudinal studies, air pollution exposures were significantly associated with fasting blood glucose levels, and both prevalent and incident DM [50–54]. A cross-sectional study of 11,847 adults in China found that exposure to elevated PM_{2.5} levels was significantly associated with increased T2DM prevalence and elevated levels of fasting glucose and HbA1c [55]. Another cross-sectional study of 15,477 participants in 33 communities in China found that PM₁, PM_{2.5}, and PM₁₀ were significantly associated with increased diabetes prevalence, and that air pollution exposure was associated with altered lipid profiles and dyslipidemias, especially among overweight or obese participants [56]. Studies elsewhere in the world examining the air pollution-diabetes association are very limited. In one of the only studies conducted in the Middle East, an analysis of 2025 participants in Jeddah, Saudi Arabia found that PM_{2.5}, especially from road dust and traffic sources, was associated with metabolic syndrome, hyperglycemia, and hypertension prevalence [57].

Several of recent studies also evaluated and identified potentially vulnerable subpopulations, although consistent evidence of effect modification is limited. Risk of diabetes associated with air pollution exposure was different across sexes [39, 50] and BMI levels [52, 56]. Studies reported elevated risks among younger populations and those with pre-diabetes and metabolic syndrome [48, 52, 56]. Dietary habits, such as fruit and alcohol consumption, also modified the air pollution-diabetes associations [42, 52, 54]. DM patients were found to be more susceptible to the air pollution-induced serum glucose variations, and Metformin treatment had a protective effect [58]. Genetic risk for T2DM may also modify susceptibility to air pollution through alternations in insulin sensitivity [46, 59].

Recent studies have also evaluated and found significant associations between diabetes risk and co-exposures, including ultrafine particles, temperature, and noise. A study of all residents residing in Toronto, Canada, found that exposures to ultrafine particles and NO₂ were significantly associated with incident diabetes [60]. PM_{2.5} was associated with risk of developing metabolic syndrome and hypertriglyceridemia, and higher levels of PM_{2.5} and temperature were both associated with elevated risk of developing elevated fasting blood glucose [61]. An analysis of a population-based cohort

in Vancouver found that diabetes incidence was associated with noise exposures, but not with traffic-related air pollutants [62]. Another analysis of a Swiss cohort did not find a relationship between NO₂ and diabetes incidence, but did find a positive association with noise exposure [63]. Analyses of two Danish cohorts also reported mixed findings regarding potential associations between noise exposure and diabetes incidence [64, 65].

Oxidative Stress as a Factor Across the Metabolic Syndrome Effects of Air Pollution

There is a strong biologic rationale for the associations between air pollution exposure and increased diabetes risk. In addition to causing harm by directly impacting our lungs, inhaling air pollutants such as PM_{2.5} and gases can induce systemic effects, including metabolic dysfunction [66]. A mediator of metabolic syndrome is insulin resistance, which relates to the development of vascular and metabolic dysfunctions that can lead to manifest cardiovascular disease and T2DM [2]. Although the exact biological mechanism(s) involved in the associations between increased air pollution exposure and greater risk of metabolic dysfunction-related diseases remain a subject of research, available evidence to date points to air pollution-induced inflammation and resulting oxidative stress as a major pathway [67].

Air pollution exposure has been found to cause oxidative stress in the body, and oxidative stress is a known risk factor for metabolic dysfunction diseases. Oxidative stress can result in lipid peroxidation, depletion of antioxidants, and activation of pro-inflammatory signaling, which can set off a cascade of biological events that can affect distant organs [68]. It contributes to many adverse health conditions, including cancer, atherosclerosis, hypertension, ischemia/perfusion, diabetes, and asthma [69]. Air pollution exposure has also been found to cause broad metabolic derangements in glucose and insulin homeostasis (including glucose intolerance, decreased insulin sensitivity, and impaired secretion) and increased blood lipid concentrations [6]. This provides biological mechanistic plausibility to the observed association between air pollution exposure and diabetes.

Of the various air pollutants, exposure to fine particulate matter (PM_{2.5}) air pollution resulting from the combustion of fossil fuels is strongly associated with the induction of both systemic inflammation and oxidative stress. The proposed mechanism is that fossil fuel particulate matter, especially coal combustion PM_{2.5}, is enriched in

both metals and sulfur [70], which can cause oxidative stress, and sulfur, which induces acidity, making the oxidative metals even more bioavailable to cause systemic damage [71]. These metals and their associated oxidative stress have been found in animal studies to mediate the adverse effects of particulate matter exposures [72].

A key test as to whether oxidative stress is the primary pathway of air pollution's effects on metabolic dysfunction-related diseases is to evaluate if diminishing oxidative stress reduces the adverse health effects of air pollution. In fact, recent considerations of dietary and genetic variant evidence validates this specific pathway's importance. Considering the large, well characterized NIH-AARP Diet and Health Cohort, Thurston et al. (2016) [73] showed PM_{2.5} exposure was related to increase risk of cardiovascular death, with subsequent analyses finding that a diet rich in anti-oxidants reduced both the diabetes and the cardiovascular mortality in this cohort [42, 74]. After adjusting for both individual- and contextual-level covariates, PM_{2.5} was found to be significantly associated with diabetes-related mortality (HR = 1.19 per 10 µg/m³; 95% CI: 1.03–1.39). However, the strength of the PM_{2.5}-diabetes mortality association was greater in subjects who consumed less than 2.5 servings of fruits per day (HR = 1.28; 95% CI: 1.08–1.53), as compared to those who consumed greater amounts (HR = 0.93; 95% CI: 0.69–1.27) (p-interaction = 0.01), for whom the PM_{2.5} effect became non-significant. Similarly, Wenton et al. (2009) [75] found that the respiratory effects of oxidative stress-inducing air pollutants were increased among elementary school children when the catalase (CAT) enzymatic (anti-oxidant) protection gene variant was absent. Thus, both the toxicology and the epidemiology of air pollution effects are consistent in indicating that oxidative stress is an important causal pathway in the associations found between air pollution exposures and increased risk of diabetes.

Future Directions

Important advances have been made in regards to our understanding of the relationship between air pollution exposure and diabetes risk during different, distinct stages of life. At the same time, oxidative stress has been identified as a risk factor for metabolic syndrome, and as an effect of air pollution exposure, especially from fossil fuel combustion particulate matter. This provides a plausible mechanism for the observed associations between air pollution and diabetes. However, this review also highlights the considerable gaps in current

knowledge, especially in regards to limited evidence examining whether early life exposures subsequently affect cardiometabolic endpoints and diabetes risk in adulthood, and the need to investigate the transgenerational effects of air pollution in the etiology of diabetes. Results from animal studies suggest this may be plausible; for example, Woodward et al. (2019) [76] reported that chronic nano-particulate matter exposure from gestation to early adulthood in male mice promoted metabolic dysregulation, food intake, and adiposity, in part through modulation of feeding behavior. Chen et al. (2018) [77] also found that prenatal exposure to diesel exhaust PM_{2.5} caused offspring β-cell dysfunction in adulthood. As established pregnancy and pediatric cohorts are followed for a longer period of time to adolescence and adulthood and exposure assessment methods continue to improve, the potential transgenerational effects will be better understood in the future. This review also found that, despite the emerging body of evidence examining the air pollution-diabetes association in Asia, studies in developing countries and other regions in the world are still very limited. Studies examining potential interactions and/or confounding effects with co-exposures such as noise and temperature are also lacking, as well as studies assessing air pollution mixtures and specific PM_{2.5} components and air pollution sources. As the built environment and neighborhood socioeconomic status are significant predictors of diabetes risk [78], their potentially interactive effects with air pollution exposure could also be examined in further detail. The emerging concept of the 'exposome,' defined as the totality of environmental exposures from conception onwards [79], could provide improved understanding of the association between multiple exposures and diabetes risk. Overall, this review provides insight into how, and to what extent, air pollution causes and exacerbates diabetes and other metabolic dysfunction-related diseases during the life-course, as well as the potential underlying pathophysiology due to oxidative stress from air pollutants.

Compliance with Ethical Standards

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Conflict of Interest The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

Appendix

Table 2 Recent studies of the association between air pollution and diabetes risk (from 2015 forward)

Reference	Study Design	Location	Sample Size	Pollutants Evaluated	Main findings
Prenatal/Gestational					
Malmqvist et al., (2015) [7•]	Observational	Skane, Sweden	84,039	NO _x , O ₃	Maternal exposure to air pollutants was associated with increased T1D risk among offspring. Highest vs lowest exposure group odds ratio of 1.62 (0.99–2.65) for O ₃ during 2nd trimester and 1.58 (1.06–2.35) for NO _x in the 3rd trimester.
Madhloum et al., (2017) [8]	Observational	Genk, Belgium	590 mother-infant pairs	PM _{2.5} , PM ₁₀ , NO ₂	Cord plasma insulin levels increased 15.5% (7.8 to 24.4) for each SD increment in PM _{2.5} levels during entire pregnancy, and effects were most pronounced during 2nd trimester; similar effects found for PM ₁₀ . Both PM _{2.5} and O ₃ exposures during 1st, 2nd, and entire pregnancy were associated with GDM.
Hu et al., (2015) [19]	Observational	Florida, U.S	410,267	PM _{2.5} , O ₃	
Pan et al., (2017) [20]	Observational	Taiwan	19,606	NO, NO ₂ , NO _x , O ₃ , SO ₂ , PM ₁₀	NO exposure during first second trimester associated with GDM in both single and two-pollutant models.
Robledo et al., (2015) [21]	Observational	U.S	219,952	PM _{2.5} , PM _{2.5} constituents, PM ₁₀ , NO _x , CO SO ₂ , O ₃	Preconception and 1st trimester maternal exposures to NO _x and SO ₂ were associated with increased risk of subsequent GDM. Preconception O ₃ was associated with lower risk of subsequent GDM. Of PM _{2.5} constituents, sulfates (preconception and 1st trimester) were negatively associated with GDM, while nitrates (1st trimester) were positively associated with GDM.
Pedersen et al., (2017) [22]	Observational	Denmark	72,745 births	NO ₂ , noise	NO ₂ exposure during 1st trimester was associated with increased risk of GDM (OR = 1.24; 1.03–1.49); effect was attenuated (OR = 1.22; 0.98–1.53) adjusting for noise.
Fleisch et al., (2016) [24]	Observational	Massachusetts, USA	159,373	PM _{2.5}	No association with GDM in the full cohort; women aged less than 20 years old had increased GDM risk with second semester PM _{2.5} exposure.
Choe et al., (2019) [23]	Observational	New York City, U.S.	256,372 births	PM _{2.5} , NO ₂	

Table 2 (continued)

Reference	Study Design	Location	Sample Size	Pollutants Evaluated	Main findings
Children/Adolescents					
Di Ciaula, (2016) [25]	Observational	Apulia, Italy	631,275	PM ₁₀ , NO _x , O ₃ , CO	1st trimester NO ₂ exposure and 2nd trimester PM _{2.5} exposure were associated with elevated GDM risk. PM _{2.5} -GDM association was elevated in younger women and non-Medicaid recipients; NO ₂ -GDM association was elevated in overweight and multiparous women.
Thiering et al., (2016) [26]	Cross-sectional	Germany	837	NO ₂ , PM ₁₀ , PM _{2.5}	NO ₂ associated with higher HOMA-IR levels.
Toledo-Corral et al., (2016) [27]	Cross-sectional	Los Angeles, California, U.S	429	PM _{2.5} , NO ₂ , NO _x	Air pollution exposure was associated with elevated fasting insulin, lower insulin sensitivity, higher acute insulin response to glucose, and higher fasting glucose in overweight/obese Latino children.
Lanzinger et al., (2018) [30]	Cross-sectional	Germany	37,372	O ₃	Inverse relationship between ozone and HbA1c levels observed in those with type 1 diabetes.
Alderete et al., (2017) [31]	Longitudinal	Los Angeles, CA, U.S	314	NO ₂ , PM _{2.5}	PM _{2.5} and NO ₂ associated with faster decline in S1 and lower S1 at age 18 years. NO ₂ associated with negatively affected beta-cell function, faster decline in disposition index and lower DI at age 18.
Beyerlein et al., (2015) [28]	Observational	Bavaria, Germany	671	PM ₁₀ , PM _{2.5} , NO ₂	Exposures to the traffic-related air pollutants PM ₁₀ , NO ₂ , and possibly PM _{2.5} accelerate the manifestation of T1D, but only in very young children.
Rosenbauer et al., (2016) [29]	Observational	North Rhine-Westphalia, Germany	6807	PM ₁₀ , NO ₂ , O ₃	Exposure to air pollution was not associated with age at onset of T1D.
Adults					
Park et al. (2015) [35]	Longitudinal	U.S	5839	PM _{2.5} and NO _x	Significant association observed with T2DM prevalence, but not incidence, in a multi-ethnic cohort.
Coogan et al. (2016) [36]	Longitudinal	U.S	43,003	NO ₂	Did not find association with diabetes incidence in a cohort of Black women.
Jerrett et al., (2017) [37•]	Longitudinal	U.S	45,231	O ₃	

Table 2 (continued)

Reference	Study Design	Location	Sample Size	Pollutants Evaluated	Main findings
Bowe et al., (2018) [6••]	Longitudinal	U.S	1,729,108	PM _{2.5}	Observed significant association between O ₃ with diabetes incidence in a cohort of Black women.
Renzi et al., (2018)	Longitudinal	Rome, Italy	1,425,580	O ₃ , PM ₁₀ , PM _{2.5-10} , PM _{2.5} , NO ₂ , and NO _x	Significant association with diabetes incidence in a cohort of U.S veterans. NO _x and O ₃ were significantly associated with diabetes incidence. The association between O ₃ and incident diabetes was stronger in women and younger (<50 years) participants.
Weinmayr et al., (2015) [39]	Longitudinal	Bochum, Essen, and Mulheim, Germany	3607	PM ₁₀ , PM _{2.5}	Increased diabetes incidence risk associated with PM ₁₀ and PM _{2.5} ; those living closer to a busy road had elevated risks.
Hansen et al. (2016) [41]	Longitudinal	Denmark	28,731	PM _{2.5} , PM ₁₀ , NO _x , NO ₂	Diabetes incidence was significantly associated with PM _{2.5} , while elevated but non-significant associations were observed with other pollutants.
Qiu et al., (2018) [50]	Longitudinal	Hong Kong	61,447	PM _{2.5}	Significant association with both diabetes prevalence and incidence.
Lim et al., (2018)	Longitudinal	U.S	549,735	PM _{2.5} , NO ₂ , O ₃	Significant association between PM _{2.5} and NO ₂ with diabetes mortality; higher associated risks among the obese and those with smaller fruit consumption.
Yitshak-Sade et al., (2015) [58]	Cross-sectional	Southern Israel	131,882	PM ₁₀ , CO, SO ₂ , O ₃ , NO ₂	NO ₂ and SO ₂ were significantly associated with increased levels of serum glucose.
Honda et al., (2017) [40]	Observational	U.S	4121	PM _{2.5} , NO ₂	PM _{2.5} and NO ₂ exposures both associated with diabetes prevalence and HbA1c levels, in both diabetic and non-diabetic participants.
Eze et al., (2016) [59]	Observational	Switzerland	1524	PM ₁₀	Significant association between diabetes and PM ₁₀ exposure; interaction observed between PM ₁₀ and genetic risk score, with odds of diabetes risk increasing per T2DM risk allele.
Chen et al., (2016)	Cross-sectional	Southern California, U.S	1023	NO ₂ , O ₃ , PM _{2.5}	Short-term PM _{2.5} exposure was associated with lower insulin sensitivity and HDL-to-LDL cholesterol ratio and higher fasting glucose and insulin,

Table 2 (continued)

Reference	Study Design	Location	Sample Size	Pollutants Evaluated	Main findings
Annual PM _{2.5} associated with higher fasting glucose, HOMA-IR, and LDL-C. Li et al., (2018) [44]	Observational	Massachusetts, US	5958	PM _{2.5} , BC, SO ₂ , NO _x , O ₃	HOMA-IR, total cholesterol, and LDL cholesterol. Living closer to a major roadway or acute exposure to traffic-related air pollutants (NO _x , BC) were significantly associated with dysregulated glucose homeostasis but not with adipokines.
Chen et al., (2016)	Longitudinal	China	27,685	PM ₁₀ , SO ₂ , NO ₂	Exposures to NO ₂ , SO ₂ , and PM ₁₀ were associated with increased fasting glucose levels in single-pollutant models.
Peng et al., (2016) [46]	Observational	Boston, Massachusetts, U.S	551	PM _{2.5}	Exposure to PM _{2.5} was associated with higher fasting glucose in a group of non-diabetics.
Yitshak-Sade et al., (2016) [49]	Longitudinal	Southern Israel	71,117	PM _{2.5} , PM ₁₀	Three-month average, but not short-term, exposure to PM ₁₀ was associated with increases in serum glucose, HbA1c, low-density lipoprotein and triglycerides, and decrease of high-density lipoprotein.
Lucht et al., (2019) [45]	Cross-sectional	Bochum, Essen, and Mulheim, Germany	4052	PM ₁₀ , PM _{2.5} , NO ₂	All pollutants were negatively associated with adiponectin and positively associated with IL-1RA and hsCRP levels; no consistent patterns with fibrinogen.
Riant et al., (2018) [47]	Cross-sectional	Northern France	2895	NO ₂ , PM ₁₀ , SO ₂	PM ₁₀ and NO ₂ associated with HbA1c increase.
Liu et al., (2016) [55]	Cross-sectional	China	11,847	PM _{2.5}	Significant associations with T2DM prevalence, fasting glucose, and HbA1c.
Wolf et al., (2016) [48]	Cross-sectional	Southern Germany	2944	PM _{2.5} , PM ₁₀ , NO ₂ , NO _x	PM _{2.5} associated with elevated HOMA-IR and insulin; NO ₂ with HOMA-IR, glucose, insulin, and leptin. Associations were higher for those with prediabetes.
Liang et al., (2019) [53]	Longitudinal	China	88,397	PM _{2.5}	Significant association with diabetes incidence. Larger effects in females, rural residents, non-smokers, younger subjects, those without hypertension, and BMI less than 25 kg/m ² .
Yang et al., (2018) [54]	Cross-sectional	China	15,477	PM ₁₀ , PM _{2.5} , PM ₁₀	

Table 2 (continued)

Reference	Study Design	Location	Sample Size	Pollutants Evaluated	Main findings
Lao et al., (2019) [52]	Longitudinal	Taiwan	147,908	PM _{2.5}	Significant associations with prevalence, fasting glucose, 2 h glucose, and 2 h insulin. Long-term PM _{2.5} exposure was associated with diabetes incidence. Those who drank occasionally/regularly or had a lower BMI (<23 kg/m ²) were more susceptible to the long-term effects of exposure to ambient PM _{2.5} .
Shamy et al., (2019) [57]	Cross-sectional	Jeddah, Saudi Arabia	2025	PM _{2.5} , PM ₁₀ and their sources	PM _{2.5} was associated with metabolic syndrome, hyperglycemia, and hypertension. PM _{2.5} from soil/road dust was associated with hyperglycemia and hypertension, and PM _{2.5} from traffic was associated with hyperglycemia.
Wallwork et al., (2016) [61]	Longitudinal	New England, U.S.	587	PM _{2.5}	PM _{2.5} was associated with elevated risk of developing metabolic syndrome, elevated fasting blood glucose level, and hypertriglyceridemia. Temperature was also associated with developing elevated fasting blood glucose level.
Bai et al., (2019) [60]	Longitudinal	Toronto, Canada	1,056,012	NO ₂ , UFP, PM _{2.5}	NO ₂ and UFP both associated with diabetes incidence.
Eze et al., (2017) [63]	Longitudinal	Switzerland	2631	NO ₂	NO ₂ exposure not associated with diabetes incidence after adjusting for noise.

References

Papers of particular interest, published recently, have been highlighted as:

- Of importance
- Of major importance

1. Teodoro JS, Varela AT, Rolo AP, Palmeira CM. High-fat and obesogenic diets: current and future strategies to fight obesity and diabetes. *Genes Nutr.* 2014 Jul;9(4):406. <https://doi.org/10.1007/s12263-014-0406-6>.
2. Cooper-DeHoff RM, Pepine CJ. Clin Cardiol. Metabolic syndrome and cardiovascular disease: challenges and opportunities. *Clin Cardiol.* 2007;30(12):593–7.
3. Hutcheson R, Rocic P. The metabolic syndrome, oxidative stress, environment, and cardiovascular disease: the great exploration. *Exp Diabetes Res.* 2012;2012:1–13.
4. 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.
5. Puett RC, Quirós-Alcalá L, Montesor-López JA, Tchangelova N, Dutta A, Payne-Sturges D, et al. Long-term exposure to ambient air pollution and type 2 diabetes in adults. *Curr Epidemiol Rep.* 2019;6:67–79.
- 6.•• Bowe B, Xie Y, Li T, Yan Y, Xian H, al-Aly Z. The 2016 Global and National Burden of Diabetes Mellitus Attributable to PM 2.5 Air Pollution. *Lancet Planet Health.* 2018;2(7):e301–122 **This study estimated the number of diabetes incidence and mortality attributable to fine particulate matter globally.**
- 7.• Malmqvist E, et al. Maternal Exposure to Air Pollution and Type 1 Diabetes – Accounting for Genetic Factors. *Environ Res.* 2015;140:268–74 **Findings from this suggest that maternal exposure to air pollution during pregnancy could increase type 1 diabetes risk among offspring.**
8. Madhloum N, et al. Cord Plasma Insulin and in Utero Exposure to Ambient Air Pollution. *Environ Int.* 2016, Elsevier;105:126–32.
9. Kim JS, et al. Longitudinal associations of in utero and early life near-roadway air pollution with trajectories of childhood body mass index. *Environ Health: Global Access Sci Source.* 2018;17(1):1, Environmental Health–10.
10. Fleisch AF, Rifas-Shiman SL, Koutrakis P, Schwartz JD, Kloog I, Melly S, et al. Prenatal exposure to traffic pollution. *Epidemiology.* Jan. 2015;26(1):43–50.
11. Fleisch AF, Luttmann-Gibson H, Perng W, Rifas-Shiman SL, Coull BA, Kloog I, et al. Prenatal and early life exposure to traffic pollution and cardiometabolic health in childhood. *Pediatr Obes.* 2017;12(1):48–57.
12. Fleisch AF, et al. Prenatal Exposure to Traffic Pollution and Childhood Body Mass Index Trajectory. *Front Endocrinol.* 2019;9:1–9.
13. van Rossem L, et al. Prenatal air pollution exposure and newborn blood pressure. *Environ Health Perspect.* 2015;123(4):353–9.
14. Zhang M, Mueller NT, Wang H, Hong X, Appel LJ, Wang X. Maternal exposure to ambient particulate matter ≤ 2.5 Mm during pregnancy and the risk for high blood pressure in childhood. *Hypertension.* 2018;72(1):194–201.
15. Breton CV, et al. Associations with newborn LINE1 and Alu methylation and childhood blood pressure and carotid intima-media thickness in the children’s health study, vol. 124; 2016. p. 1905–12.
16. Angueira AR, Ludvik AE, Reddy TE, Wicksteed B, Lowe WL, Layden BT. New insights into gestational glucose metabolism: lessons learned from 21st century approaches. *Diabetes.* 2015;64(2): 327–34.
17. Casagrande SS, Linder B, Cowie CC. Prevalence of gestational diabetes and subsequent type 2 diabetes among US women. *Diabetes Res Clin Pract.* 2018;141:200–8.
18. Buchanan TA, Xiang AH, Page KA. Gestational diabetes mellitus: risks and management during and after pregnancy. *Nat Rev Endocrinol.* 2012;8(11):639–49.
19. Hu H, Ha S, Henderson BH, Warner TD, Roth J, Kan H, et al. Association of atmospheric particulate matter and ozone with gestational diabetes mellitus. *Environ Health Perspect.* 2015;123(9): 853–9.
20. Pan SC, Huang CC, Lin SJ, Chen BY, Chan CC, Guo YLL. Gestational diabetes mellitus was related to ambient air pollutant nitric oxide during early gestation. *Environ Res.* 2017;158:318–23.
21. Robledo CA, Mendola P, Yeung E, Männistö T, Sundaram R, Liu D, et al. Preconception and early pregnancy air pollution exposures and risk of gestational diabetes mellitus. *Environ Res.* 2015;137: 316–22.
22. Pedersen M, Olsen SF, Halldorsson TI, Zhang C, Hjortebjerg D, Ketzel M, et al. Gestational diabetes mellitus and exposure to ambient air pollution and road traffic noise: a cohort study. *Environ Int.* 2017;108(August):253–60.
23. Choe SA, Eliot MN, Savitz DA, Wellenius GA. Ambient air pollution during pregnancy and gestational diabetes in new York City. *Environ Res.* 2019;175:414–20.
24. Fleisch AF, et al. Air pollution exposure and gestational diabetes mellitus among pregnant women in Massachusetts: a cohort study. *Environ Health: Global Access Sci Source.* 2016;15(1):1, Environmental Health–9.
25. Di C. Agostino. “Type I diabetes in Paediatric age in Apulia (Italy): incidence and associations with outdoor air pollutants.” diabetes research and clinical practice. Elsevier Ireland Ltd. 2016;111:36–43.
26. Thiering E, Markevych I, Brüske I, Fuertes E, Kratzsch J, Sugiri D, et al. Associations of residential long-term air pollution exposures and satellite-derived greenness with insulin resistance in German adolescents. *Environ Health Perspect.* 2016;124(8):1291–8.
27. Toledo-Corral CM, Alderete TL, Habre R, Berhane K, Lurmann FW, Weigensberg MJ, et al. Effects of air pollution exposure on glucose metabolism in Los Angeles minority children. *Pediatr Obes.* 2018;13(1):54–62.
28. Beyerlein A, et al. Ambient air pollution and early manifestation of type 1 diabetes. *Epidemiology.* 2015;26(3):e31–2.
29. Rosenbauer J, Tamayo T, Bächle C, Stahl-Pehe A, Landwehr S, Sugiri D, et al. Re: ambient air pollution and early manifestation of type 1 diabetes. *Epidemiology.* 2016;27(4):e25–6.
30. Lanzinger S, Rosenbauer J, Sugiri D, Schikowski T, Treiber B, Klee D, et al. Impact of long-term air pollution exposure on metabolic control in children and adolescents with type 1 diabetes: results from the DPV registry.” *Diabetologia.* 2018;61(6):1354–61.
- 31.•• Alderete TL, Habre R, Toledo-Corral CM, Berhane K, Chen Z, Lurmann FW, et al. Longitudinal Associations between Ambient Air Pollution with Insulin Sensitivity, Beta-Cell Function, and Adiposity in Los Angeles Latino Children. *Diabetes.* 2017;66(7): 1789–96. <https://doi.org/10.2337/db16-1416> **This study is one of the few longitudinal investigations examining associations between air pollution exposure and cardiometabolic biomarkers; long-term exposure to air pollutants accelerated declines in insulin sensitivity and beta-cell function among overweight and obese children.**
32. Jerrett M, McConnell R, Wolch J, Chang R, Lam C, Dunton G, et al. Traffic-related air pollution and obesity formation in children: a longitudinal, multilevel analysis. *Environ Health.* 2014;13(1):49.
33. Pieters N, Koppen G, Van Poppel M, De Prins S, Cox B, Dons E, et al. Blood pressure and same-day exposure to air pollution at school: associations with nano-sized to coarse PM in children. *Environ Health Perspect.* 2015;123(7):737–42.

34. Dong GH, Wang J, Zeng XW, Chen L, Qin XD, Zhou Y, et al. Interactions between air pollution and obesity on blood pressure and hypertension in Chinese children. *Epidemiology*. 2015;26(5):740–7.
35. Park SK, et al. Long-term exposure to air pollution and type 2 diabetes mellitus in a multiethnic cohort. *Am J Epidemiol*. 2015;181(5):327–36.
36. Coogan PF, et al. Long Term Exposure to NO₂ and Diabetes Incidence in the Black Women's Health Study. *Environ Res*. 2016;148(2, Elsevier):360–6.
37. Jerrett M, et al. "Ambient ozone and incident diabetes: a prospective analysis in a large cohort of African American women." *Environ Int*. 2017;102:42–47. **This is one of the only studies linking long-term ozone exposures with diabetes incidence.**
38. Renzi M, et al. Air pollution and occurrence of type 2 diabetes in a large cohort study. *Environ Int*. 2017;112(December):68–76.
39. Weinmayr G, et al. Long-term exposure to fine particulate matter and incidence of type 2 diabetes mellitus in a cohort study: effects of Total and traffic-specific air pollution. *Environ Health: Global Access Sci Source*. 2015;14(1):1–8.
40. Honda T, Pun VC, Manjourides J, Suh H. Associations between long-term exposure to air pollution, glycosylated hemoglobin and diabetes. *Int J Hyg Environ Health*. 2017;220(7):1124–32.
41. Hansen AB, et al. Long-Term Exposure to Fine Particulate Matter and Incidence of Diabetes in the Danish Nurse Cohort. *Environ Int*. 2016;91, The Authors:243–50.
42. Lim CC, Hayes RB, Ahn J, Shao Y, Silverman DT, Jones RR, et al. Association between long-term exposure to ambient air pollution and diabetes mortality in the US. *Environ Res*. 2018;165:330–6.
43. Chen Z, Salam MT, Toledo-Corral C, Watanabe RM, Xiang AH, Buchanan TA, et al. Ambient air pollutants have adverse effects on insulin and glucose homeostasis in mexican americans. *Diabetes Care*. 2016;39:547–54.
44. Li W, Dorans KS, Wilker EH, Rice MB, Kloog I, Schwartz JD, et al. Ambient air pollution, adipokines, and glucose homeostasis: the Framingham heart study. *Environ Int*. 2018;111:14–22.
45. Lucht S, et al. Air Pollution and Diabetes-Related Biomarkers in Non-Diabetic Adults: A Pathway to Impaired Glucose Metabolism? *Environ Int*. 2019;124(September 2018, Elsevier):370–92.
46. Peng C, 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.
47. Riant M, Meirhaeghe A, Giovannelli J, Occelli F, Havet A, Cuny D, et al. Associations between long-term exposure to air pollution, glycosylated hemoglobin, fasting blood glucose and diabetes mellitus in northern France. *Environ Int*. 2018;120:121–9.
48. Wolf K, et al. Association between long-term exposure to air pollution and biomarkers related to insulin resistance, subclinical inflammation and Adipokines. *Diabetes*. 2016;65(November):db151567.
49. Yitshak Sade M, et al. The association between air pollution exposure and glucose and lipids levels. *J Clin Endocrinol Metab*. 2016;101(6):2460–7. <https://doi.org/10.1210/jc.2016-1378>.
50. Qiu H, Schooling CM, Sun S, Tsang H, Yang Y, Lee RSY, et al. Long-term exposure to fine particulate matter air pollution and type 2 diabetes mellitus in elderly: a cohort study in Hong Kong. *Environ Int*. 2018;113:350–6.
51. Li S, et al. Air Pollution and Fasting Blood Glucose: A Longitudinal Study in China. *Sci Total Environ*. 2015;541(2, Elsevier B.V.):750–5.
52. Lao, Xiang Qian, et al. Long-term exposure to ambient fine particulate matter (PM_{2.5}) and incident type 2 diabetes : a longitudinal cohort study. *Diabetologia*, 2019;62:1–1.
53. Liang F, Yang X, Liu F, Li J, Xiao Q, Chen J, et al. Long-term exposure to ambient fine particulate matter and incidence of diabetes in China: a cohort study. *Environ Int*. 2019;126:568–75.
54. Yang Y, Guo Y, Qian ZM, Ruan Z, Zheng Y, Woodward A, et al. Ambient fine particulate pollution associated with diabetes mellitus among the elderly aged 50 years and older in China. *Environ Pollut*. 2018;243:815–23.
55. Liu C, 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, Elsevier Ltd:416–21.
56. Yang B-Y, Qian Z(M), Li S, Chen G, Bloom MS, Elliott M, et al. Ambient air pollution in relation to diabetes and glucose-homoeostasis markers in China: a cross-sectional study with findings from the 33 communities Chinese health study. *Lancet Planet Health*. 2018;2(2, The Author(s). Published by Elsevier Ltd. This is an Open Access article under the CC BY-NC-ND 4.0 license):e64–73.
57. Shamy M, Alghamdi M, Khoder M, Mohorjy A, Alkhatim A, Alkhalaf A, et al. Association between exposure to ambient air particulates and metabolic syndrome components in a Saudi Arabian population. *Int J Environ Res Public Health*. 2017;15(1):27.
58. Yitshak-Sade M, et al. Air pollution and serum glucose levels. *Medicine (United States)*. 2015;94(27):e1093.
59. Eze IC, et al. Air Pollution and Diabetes Association: Modification by Type 2 Diabetes Genetic Risk Score. *Environ Int*. 2016;94, The Authors:263–71.
60. Bai L, Chen H, Hatzopoulou M, Jerrett M, Kwong JC, Burnett RT, et al. Exposure to ambient ultrafine particles and nitrogen dioxide and incident hypertension and diabetes. *Epidemiology*. 2018;29:323–32.
61. Wallwork RS, et al. Ambient fine particulate matter, outdoor temperature, and risk of metabolic syndrome. *Am J Epidemiol*. 2016;185:30–9.
62. Clark C, Sbihi H, Tamburic L, Brauer M, Frank LD, Davies HW. Association of long-term exposure to transportation noise and traffic-related air pollution with the incidence of diabetes: a prospective cohort study. *Environ Health Perspect*. 2017;125(1–10):087025.
63. Eze IC, Foraster M, Schaffner E, Vienneau D, Héritier H, Rudzik F, et al. Long-term exposure to transportation noise and air pollution in relation to incident diabetes in the SAPALDIA study. *Int J Epidemiol*. 2017;46(4):1115–25.
64. Roswall N, Raaschou-Nielsen O, Jensen SS, Tjønneland A, Sørensen M. Long-term exposure to residential railway and road traffic noise and risk for diabetes in a Danish cohort. *Environ Res*. 2018;160:292–7.
65. Jørgensen JT, et al. Long-term exposure to road traffic noise and incidence of diabetes in the Danish nurse cohort. *Environ Health Perspect*. 2019;127(5):057006.
66. Alderete TL, Chen Z, Toledo-Corral CM, Contreras ZA, Kim JS, Habre R, et al. Ambient and traffic-related air pollution exposures as novel risk factors for metabolic dysfunction and type 2 diabetes. *Curr Epidemiol Rep*. 2018;5:79–91.
67. Rajagopalan S, Brook RD. Air pollution and type 2 diabetes: mechanistic insights. *Diabetes*. 2012;61(12):3037–45.
68. Birben E, Sahiner UM, Sackesen C, Erzurum S, Kalayci O. Oxidative stress and antioxidant defense. *World Allergy Organ J*. 2012;5(1):9–19.
69. Schraufnagel DE, Balmes JR, Cowl CT, De Matteis S, Jung SH, Mortimer K, Perez-Padilla R, Rice MB, Riojas-Rodriguez H, Sood A, Thurston GD, To T, Vanker A, Wuebbles DJ. Air pollution and noncommunicable diseases: a review by the forum of international respiratory Societies' environmental committee, part 1: the damaging effects of air pollution. 2018;155:417–426

70. Reddy MS, Basha S, Joshi HV, Jha B. Evaluation of the emission characteristics of trace metals from coal and fuel oil fired power plants and their fate during combustion. *J Hazard Mater.* 2005;123(1–3):242–9.
71. Duffin R, Mills NL, Donaldson K. Nanoparticles—a thoracic toxicology perspective. *Yonsei Med J.* 2007;48:561–72.
72. Costa DL, Dreher KL. Bioavailable transition metals in particulate matter mediate cardiopulmonary injury in healthy and compromised animal models. *Environ Health Perspect.* 1997;105 Suppl 5:1053–60.
73. Thurston GD, Ahn J, Cromar KR, Shao Y, Reynolds HR, Jerrett M, et al. Ambient particulate matter air pollution exposure and mortality in the NIH-AARP diet and health cohort. *Environ Health Perspect.* 2015;124(4):484–90.
74. Lim CC, Hayes RB, Ahn J, Shao Y, Silverman DT, Jones RR, Thurston GD. Mediterranean diet and the association between air pollution and cardiovascular disease mortality risk. *Circulation.* 2019;139:1766–1775
75. Wenten M, et al. Functional variants in the catalase and myeloperoxidase genes, ambient air pollution, and respiratory-related school absences: an example of epistasis in gene-environment interactions. *Am J Epidemiol.* 2009;170(12):1494–501.
76. Woodward NC, Crow AL, Zhang Y, Epstein S, Hartiala J, Johnson R, et al. Exposure to nanoscale particulate matter from gestation to adulthood impairs metabolic homeostasis in mice. *Sci Rep.* 2019;9:1816.
77. Chen M, Liang S, Qin X, Zhang L, Qiu L, Chen S, et al. Prenatal exposure to diesel exhaust PM_{2.5} causes offspring β cell dysfunction in adulthood. *Am J Physiol Endocrinol Metab.* 2017;315(1):E72–80.
78. Bilal U, Auchincloss AH, Diez-Roux AV. Neighborhood environments and diabetes risk and control. *Curr Diab Rep.* 2018;18:62.
79. Vrijheid M, Slama R, Robinson O, Chatzi L, Coen M, Van den Hazel P, et al. The human early-life exposome (HELIX): project rationale and design. *Environ Health Perspect.* 2014;122(6):535–44.

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