Ambient Environment and the Epidemiology of Preterm Birth

Gary M. Shaw, DrPH[a,*], David.J.X. Gonzalez, PhD[b], Dana E. Goin, PhD[c], Kari A. Weber, PhD, MHS[d], Amy M. Padula, PhD[e]

KEYWORDS

• Prematurity • Environment • Risk factors • Epidemiology
• Gene–environment interactions

KEY POINTS

- Environmental chemical and physical exposures have been associated with increased risks of preterm birth (PTB).
- Chemical and physical exposures during pregnancy may derive from air pollutants, water contaminants, and other sources in proximity to residential addresses.
- Numerous studies have examined the role of single environmental exposures in influencing PTB risk, but few studies have attempted to account for the complexities of multiple exposures — the exposome.
- Factors that modify risks of the exposome, including variations associated with the structural genome, epigenome, social stressors, and dietary factors, will be important to explore in the future.

INTRODUCTION

Preterm birth (PTB, delivery before 37 weeks of gestation) is associated with substantial morbidity and mortality with a global burden of greater than 15 million babies born preterm every year.[1,2] In the United States, PTB occurs in approximately 10% of all

[a] Epidemiology and Population Health, Obstetrics & Gynecology – Maternal Fetal Medicine, Department of Pediatrics, Stanford University School of Medicine, Center for Academic Medicine (CAM), 453 Quarry Road, Stanford, CA 94304, USA; [b] Division of Environmental Health Sciences, School of Public Health, University of California, 2121 Berkeley Way, CA 94720, USA; [c] Department of Epidemiology, Mailman School of Public Health, Columbia University, 722 West 168th Street, New York, NY 10032, USA; [d] Department of Epidemiology, Fay W. Boozman College of Public Health, University of Arkansas for Medical Sciences, 4301 West Markham Street, RAHN 6219, Rock, AR 72205, USA; [e] Department of Obstetrics, Gynecology and Reproductive Sciences, University of California San Francisco, 490 Illinois Street, #103N, San Francisco, CA 94158, USA
* Corresponding author.
E-mail address: gmshaw@stanford.edu

Clin Perinatol 51 (2024) 361–377
https://doi.org/10.1016/j.clp.2024.02.004
perinatology.theclinics.com

livebirths.[3,4] Frequency of PTB in the United States is higher than what is observed in other industrialized countries, for example, Canada (7%) and France (6%).[5] Despite medical advances, the frequency of PTB has increased in the United States for decades.[3] Part of the overall occurrence of PTB can be attributed to medical interventions to facilitate earlier delivery when there are complications endangering the health of the pregnant person or fetus. However, risk factors for the largest population burden of PTB, *spontaneous* PTB (sPTB), remain largely unexplained.

PTB is a complex phenomenon and not well understood as a singular condition defined simply by the arbitrary dichotomy of birth at less than 37 completed weeks of gestation (vs $\geq$37 weeks).[6] Our current etiologic understanding is somewhat hampered by the fact that no nonprimate experimental model exists that is sufficiently informative of the human condition of PTB. Thus, epidemiologic studies must be a critical part of our toolkit in solving the substantive problem of PTB. In experimental studies, the investigator has more "control" over the many exposures study subjects may encounter; whereas, in epidemiologic studies, the investigator is relegated to being an "observer" of what and how individuals in a study population are exposed to and affected by potential risk factors. In some instances, exposures may not be known or cannot be adequately controlled for. This may be a particular challenge to investigations involving environmental factors.

Our goal here is not to provide a comprehensive review of past epidemiologic work, but rather to capture the essence of the manifold environmental factors that have been observed to influence the risks of PTB. Although "environment" can be defined broadly as nongenetic in nature, the bulk of our focus will be on potential exposures associated with an individual's residential *ambient* environment and following with a brief overview of some of the other nongenetic risk factors such as demographic, substance use, nutritional, and stress studied for their association with PTB. These other nongenetic factors could be the subject of lengthy reviews on their own and are noted in brief here owing to their pertinence in the examination of risks associated with exposures in the ambient environment.

SELECT NONGENETIC FACTORS

Demographics

One of the strongest associations for PTB observed in the United States is the elevated risks of PTB that African American or Black women experience.[7,8] While Hispanics and Asians appear to have somewhat lowered risks of PTB relative to non-Hispanic Whites, African Americans have approximately double the risk of PTB compared with non-Hispanic Whites. This risk is approximately 3 fold for African Americans compared with non-Hispanic Whites for PTB before 28 weeks.[9] This Black–White risk disparity was comprehensively examined by a working group commissioned by the March of Dimes a few years ago.[7] The working group considered 33 hypothesized causes for their potential plausibility to contribute to the risk disparity and concluded *"Racism is a highly plausible, major upstream contributor to the Black-White disparity in PTB through multiple pathways and biological mechanisms."* Racism has been associated with numerous contributory risk factors, including socioeconomic disadvantage, chronic stress, and potentially harmful ambient environmental exposures.[10–12]

With respect to other demographic characteristics, younger maternal age (<20 years) and older maternal age (>35 years) have been associated with increased risk of PTB.[6] Multifetal pregnancy has been associated with increased PTB risk.[3] Increased risks of PTB have been observed for male offspring,[13] particularly those that occur before 28 weeks of gestation.[14]

Substance Use

Although cigarette smoking has been associated with several outcomes of pregnancy (eg, reduced birthweight), the association of cigarette smoking with PTB risk is modest and has not been consistently observed.[6] Similarly, the use of alcohol and caffeine has not revealed consistent associations with PTB.[6] The use of cocaine during pregnancy has shown consistent evidence of approximately a 2 fold increased risk of PTB.[6] Other substance use in pregnancy including opioids,[15] methamphetamines,[16] and cannabis[17] has been associated with increased PTB risk.

Nutrition

Dietary quality as well as specific nutrient intakes has been explored for their association with PTB, although consistent results have generally not been observed. Diets including more fruits, vegetables, whole grains, poultry, and fish have been associated with reduced PTB risk.[18] Some studies have reported the reduced risks of PTB associated with pre- and antenatal intake of folic acid.[19–22] An increased intake of iron, zinc, omega-3, omega-6, vitamin D, calcium, and magnesium[19,23] has been observed to decrease PTB risk. Higher levels of antioxidants such as carotenoids have been associated with a reduced risk of PTB.[24] Some findings indicate that probiotic dairy product intake may be associated with a reduced risk of PTB.[25] Other nutritional aspects that have been observed to increase the risk for PTB include both low and elevated prepregnancy body mass index.[26–28] Diabetes has also been associated with PTB risk.[29] Interestingly, recent findings have observed that PTB risk increases with elevated serum glucose levels during mid-pregnancy, but well short of levels seen in overt diabetes.[30]

Interpregnancy Interval

A short interpregnancy interval (IPI) (<6 months) between delivery of one pregnancy and conception of the next has been associated with adverse pregnancy outcomes, including PTB in numerous populations,[31–33] though it does not appear to contribute to the Black–White disparity in PTB risk.[34] The underlying explanation to a shortened IPI association is unknown with suggestions including potential confounding,[35] low nutrient levels such as lower folic acid,[36] and variation in microbiota taxa.[37]

Stress

Indicators of both biologic and psychosocial stress have been studied for their contributions to PTB risk.[38] Corticotrophin-releasing hormone, cortisol, other biomarkers of stress, as well as a variety of indicators of perceived stress (eg, life events) have been measured. Approaches employed thus far have produced what many investigators might conclude as being mixed results. A biomarker study that measured urinary catecholamines (dopamine, epinephrine, and norepinephrine), that is, biomarkers of stress, showed a 2- to 4-fold elevation for PTB among those with the highest urinary levels in mid-pregnancy.[39] A well-conducted Canadian study[40] investigated a sizable number of stress indicators and measures of psychological distress as predictors of sPTB. A woman's reported pregnancy-related anxiety (odds ratio = 1.8) was observed to be associated with PTB. The phenomenon of pregnancy-related anxiety has since been recapitulated as a PTB risk factor employing machine learning analytics.[41]

AMBIENT ENVIRONMENTAL FACTORS AND PRETERM BIRTH RISK

Here, we highlight aspects of the ambient environment that have been investigated for their influence on risk of PTB. By ambient, we definitionally focus on those aspects of the environment that are proximal to where a pregnant individual may reside. A

discussion of possible occupational risks for PTB such as long working hours, shift work, physical labor, and chemical exposures is outside the ambit of this narrative, but an entry point into that literature can be found elsewhere.[42] Similarly, previous reviews have summarized associations between classes of environmental chemicals and PTB.[22]

Air Pollution

Air pollutants may be one of the most studied exposures associated with the ambient environment for risk of PTB. Most regularly monitored air pollutants (ie, nitrogen dioxide [NO_2], carbon monoxide, sulfur dioxide, ozone, and particulate matter) have been associated with PTB, but most consistent evidence for an association has been found with particulate matter with a diameter less than 2.5 μm ($PM_{2.5}$), which can penetrate the lung and enter the bloodstream. It has been estimated that 2.8 to 5.9 million PTBs may be associated with $PM_{2.5}$ exposure globally.[43] In a recent review, exposure to $PM_{2.5}$ was associated with an increased risk of PTB in 19 of 24 studies (79%).[44] A comprehensive review of air pollution and pregnancy outcomes found that exposure to $PM_{2.5}$ over the entire pregnancy was significantly associated with higher risk for PTB: the pooled odds ratio was a 1.24 per 10 $\mu g/m^3$ increase in $PM_{2.5}$ during the entire pregnancy.[45] High levels of $PM_{2.5}$ in the second trimester and at the end of pregnancy are the most critical periods[46] and associations are stronger for earlier PTB.[46] Notably, associations between air pollution and PTB have been stronger in neighborhoods with lower socioeconomic status (SES).[47]

Wildfires

Although there have been many studies on air pollution in general, the few studies on wildfire smoke and PTB had diverse methods and inconsistent results. A recent review[48] found 2 of 4 studies with evidence of associations between wildfire smoke and PTB. These studies have been conducted all over the world from wildfires in the western United States,[49,50] forest fires in South America,[51] and bushfires in Australia[52] with various exposure assessment methods. The largest study to date examined approximately 3 million births in California between 2006 and 2012 and found that each day of exposure to any wildfire smoke was associated with a 0.49% increase in risk of PTB.[50] Annual percentages of PTBs in California attributable to wildfire smoke between 2007 and 2012 ranged from 1.8% in 2011 to 6.3% in 2008, a high wildfire year.[50] The effect of stress due to the wildfire event has been associated with maternal mental health[53] and may be an additional pathway by which wildfires may affect PTB.

Greenspace

A recent area of study is proximity to greenspace and lowered risk of pregnancy outcomes.[54] Most studies that have explored PTB risk have employed the Normalized Difference Vegetation Index (NDVI), an index derived using remote sensing. The results have been inconsistent and have varied depending on the residential buffer used (ie, the concentric area around one's residential address used to determine greenspace exposure), environmental or socioeconomic factors that were adjusted for, and size of the study population. For example, one study of roughly 3 million births in Texas did not observe any associations between a higher residential NDVI in a 250 meter buffer and PTB after adjustment for individual and neighborhood factors.[55] A California study observed a decreased risk of selected subphenotypes of PTB (eg, <28 weeks of gestation) with higher residential NDVIs across all buffers (250, 500, 1000, and 2000 meters) with the strongest associations in the largest buffers.[56] These

investigators also observed statistical interaction between NDVI and various measures of air pollution indicating the highest risk may be among those in areas with low residential greenspace and high air pollution.[56] Another California study observed an inverse association between more greenness and PTB risk in the largest examined residential buffers and after adjustment for certain air pollution measures, but not in the smaller residential buffers (50 meters).[57] A study in Rhode Island observed an association between NDVI and PTB birth, but it was attenuated after adjustment for SES.[58] A study in Pennsylvania adjusting for other environmental as well as demographic and clinical factors observed an inverse association between higher NDVI and PTB only in cities.[59] A study in Vancouver, Canada observed those in the highest quartile of residential NDVI within 100 meter buffers to have a lower odds of PTB compared with those in the lowest quartile and adjustment for other environmental factors such as air pollution, and noise did not meaningfully impact the associations.[60] Unraveling the beneficial mechanisms of greenspace to determine the most appropriate buffers and factors to adjust for may lead to more consistent associations.

Extreme Heat

An area of increasing focus, particularly due to climate change, has been the potential risks associated with heat waves. In a recent review, Dalugoda and colleagues[61] noted that 23 of 30 studies showed elevated temperatures to be associated with increased PTB risks. However, inferences from this body of work are challenged by the fact that extreme heat exposure has been variably defined based on temperature (eg, mean, maximum, or upper percentiles), duration at that temperature (eg, 2–7 days), and the investigated gestational timing of exposure. The biologic mechanisms that may underly an association between extreme heat and PTB risk are not well understood and will require further investigation. Although some studies have explored interactions between extreme heat and air pollutants, more efforts will be needed to determine the potential modifying influence one may have on the other. Interestingly, extreme heat exposure and PTB risk have recently been observed to be influenced by the levels of greenness and SES.[62] Of note, exposure to cold temperatures has also been associated with increased PTB risk.[63]

Oil and Gas Development

There is widespread residential exposure to oil and gas development in major petroleum producing countries such as the United States, where 17.6 million residents live within 1.6 km (1 mile) of active wells.[64] Numerous studies have investigated the association between PTB and proximity to such wells using data from the United States and Canada.[59,65–74] Drilling and operating oil and gas wells is associated with air pollutant emissions, water contamination, soil contamination, and noise pollution.[75] Researchers have observed elevated concentrations of pollutants known to be associated with PTB risk, such as $PM_{2.5,}$ ozone, and being downwind of new and active wells.[76] Consequently, researchers working in this area have used proximity to wells as a metric for the complex mixture of physical and psychosocial stressors associated with oil and gas production.[77]

Most of the epidemiologic studies have reported positive associations between higher PTB risk and exposures to oil and gas development during gestation.[59,67,68,72,73,78,79] Four studies did not observe an association between exposures to oil and gas development and PTB risk,[66,70,71,74] and another study using data from Colorado found an inverse association between exposure to oil and gas development and PTB risk.[69] Most of these studies investigated exposures to unconventional (ie, hydraulically fractured) or conventional oil and gas wells. One study investigated exposures to natural gas

flaring, where excess gas is combusted in situ, and found significantly higher PTB risk for those exposed during pregnancy.[65] More work is needed to investigate specific etiologic pathways by which exposures to oil and gas development confer risk of PTB.[77]

Pesticides

Several pesticides are known reproductive toxicants.[80] Despite this evidence and substantial concern from the public about potential reproductive risks, relatively few studies have investigated potential associations between exposures to specific pesticides and most reproductive outcomes including PTB. Suggested potential mechanisms for an association between pesticide exposures and PTB have included placental compromise with downstream alterations in nutrient transfer,[81] elevated oxidative stress,[82] and hormonal dysfunction.[83] The few studies that have explored this broad question of various pesticide compounds and PTB have observed inconsistent results.[84–89] Not unlike other environmental epidemiology studies, studies involving pesticide exposures have been limited by the exposure assessment used, the study design employed as well as small study population size, each of these limitations serving to challenge clear inferences to be drawn. Measures of exposure have included individual-level estimations such as serum measures of dichlorodiphenyldichloroethylene (DDE)[90] or chlordecone,[91] ecologic-level estimations such as county-level pesticide use,[86,92] and residential addresses of individuals and their proximity to pesticide applications.[93] Serum levels of dichlorodiphenyltrichloroethane (DDT)/DDE have been associated with increased PTB risks but not in all studies particularly in more recent studies where serum levels have been decreasing.[84]

Of note, a recent study in a highly agricultural region of California examined associations between a woman's residential proximity to agriculture-related pesticide applications during pregnancy and risk of sPTB[93] and preeclampsia (a major contributor to medically indicated PTB).[94] Despite a very large study population, consideration of narrowly defined phenotypes, and consideration of a variety of gestational exposure definitions such as chemical groups, specific chemicals, and number of pesticides, there was a notable lack of association between pesticide exposures and elevated risk of either sPTB or preeclampsia. Owing to some results showing decreased risks with exposures, the investigators speculated the possibility that unobserved early fetal loss hindered the ability to derive unbiased risk estimates. That is, pesticide exposures in pregnancies before 20 weeks, the earliest a birth would be identified in vital statistics files and before preeclampsia would be diagnosed, may selectively increase the odds of earlier losses in pregnancies destined to be preterm or preeclamptic and therefore not observable when only live birth data are used for the target study population.

Drinking Water Constituents

Other potential putative exposures in the environment such as water constituents have been investigated.[84,95] Previous studies have shown higher risk of PTB when there was worse overall drinking water quality or a violation of a maximum contaminant level for any contaminant in drinking water during pregnancy.[96] However, specific types of drinking water contamination (organic, inorganic, biological, and radiological[97]) are less studied and work that does exist shows inconsistent relationships. For example, organic contaminants include pharmaceuticals and personal care products, endocrine-disrupting chemicals, pesticides, and flame retardants[98] and can get into both surface and groundwater through leaking of industrial and domestic waste. Despite these broad categories, only atrazine (an herbicide) in drinking water has been well-studied with respect to PTB, but the results are inconsistent: one study

showed a positive relationship[86] and others showed null or imprecise results.[99] Trihalomethanes are formed when organic matter in the water interacts with the chlorine used to disinfect it. Some investigators have found modest associations of disinfection byproducts with the risk of PTB,[100] while others have not.[101] Inorganic contamination includes trace elements such as arsenic, barium, cadmium, lead, and vanadium. There is more evidence linking inorganic contaminants in drinking water with an increased risk of PTB, especially for arsenic[102] and nitrates.[103–106] Biological contamination can occur when there is an excess of algae, pathogenic bacteria, or viruses in the water. This is also usually a result of animal waste or industrial pollution entering the water source. Very little evidence exists regarding biological contamination of drinking water and risk of PTB. Radiological contamination occurs when radioactive minerals in the ground, such as radium and uranium, or radon gas, release radiation into the water. Only uranium in drinking water has been linked with an increased risk of PTB.[107] While evidence exists regarding maternal exposure to specific water contaminants during pregnancy, establishing drinking water as the source of exposure is difficult given the challenges in obtaining accurate exposure measurements.

Proximity to Point Source Emissions

Studies have observed modestly elevated PTB risks associated with residential proximity to petroleum industries[108,109] as well as to cement manufacturing[110] and electrical generation associated with coal emissions.[111] Residential proximity to waste sites has also been explored for associations with PTB. Potential exposure to waste site contamination varies based on what materials have been disposed of at the particular landfill. The limited studies of this potential hazard have generally showed null or small increased PTB risks.[84]

Residential exposures to concentrated animal feeding operations (CAFOs) (facilities that confine animals at high densities for prolonged periods of time) have been associated with decreased birthweight and shortened gestational time with closer distance between maternal residential address and poultry.[112]

Residential proximity to aircraft noise has been observed to increase PTB risk and that risk may be further amplified with exposures to traffic-related air pollutants.[113] Other sources of noise such as traffic on roads have also been observed to be associated with PTB risk.[114] Noise has been hypothesized to biologically increase stress.[115]

Other Environmental Exposures

Environmental-related exposures to various chemicals and risk of PTB have been explored. Elevated PTB risks associated with maternal exposures to lead have been observed. Exposures as measured in blood to lead and arsenic were recently observed to increase the risk of preeclampsia with inverse modifying influences from manganese.[116] Studies of exposures to polychlorinated biphenyls have generally not observed elevated PTB risks.[84]

Perfluoroalkyl and polyfluoroalkyl substances (PFAS) are extremely persistent chemicals in the environment based on their widespread usage to enable nonstick, waterproof, and stain-resistant coatings to a variety of consumer products, including cookware, food packaging, clothing, carpeting, cosmetics, and textiles. Exposures to these chemicals have been associated with shorter gestational length.[117,118]

Polycyclic aromatic hydrocarbons (PAHs), contaminants produced from combustion of fossil fuels and other sources, have been associated with an increased risk of PTB.[46,119]

Owing to their reproductive toxicity, endocrine disrupting chemicals have been investigated for possible increased PTB risk. Two broad chemical groupings most

studied are phthalates and phenols. Interestingly, Chin and colleagues[120] observed that higher urinary concentrations of low molecular weight phthalates increased gestational length, whereas higher concentrations of higher molecular weight phthalates decreased gestational length. Recently, Zhang and colleagues[121] observed that combined levels as measured in urine of phthalates and phenols (bisphenol specifically) preconceptionally in both men and women were associated with an increased risk of PTB.

GENOMIC–ENVIRONMENT INTERACTIONS

Host susceptibility plays a role in PTB risk, evidenced, for example, by familial aggregation (mothers, sisters, and daughters share risks) and by variability across population subgroups and an individual's response to stressors and infections. Several genome-wide investigations have identified genetic variants that contribute to a modest proportion of the incidence of PTB. There are numerous gaps in our understanding of the genetic contributions to PTB — many of which have been nicely discussed by Jain and colleagues[122] One particular gap that will be important to fill is the need for more investigation of potential gene–environment interactions on risk of PTB. Such studies will better define possible at-risk loci as well as better define environmental exposure parameters that result in risk.

An overall pattern of results where various exposures, demographic factors, and genetic variants seem to insufficiently account for differences in disease risk, has led many to posit that individual *epigenetic* variability may underly etiology. DNA methylation is one of the most studied components of epigenesis. Variations in DNA methylation can be influenced by environmental exposures such as air pollutants, cigarette smoking, and stress associated with social context.[123–125]

Investigations have explored epigenetics and PTB.[122,126] In general, the extant literature indicates that findings are supportive for an association between epigenetics and PTB. Evidence of differential susceptibility to the air pollutants NO_2 and ozone via methylation changes (in placental and cord blood tissues) has been observed by Ladd-Acosta and colleagues.[125] Furthermore, an association has been reported between social support and alterations in DNA methylation on risk of PTB.[123] In their study population of the Boston Birth Cohort of 250 African American mothers, Surkan and colleagues[123] observed that the absence of support from the baby's father was associated with maternal DNA methylation changes in selected genes and a lack of support from family and friends was associated with maternal DNA hypermethylation on multiple genes. This study provides intriguing results suggesting biological embedding of social support during pregnancy on maternal DNA methylation. That group has also demonstrated an association between smoking during pregnancy, alterations in DNA methylation, and fetal development.[124]

Given that variations in DNA methylation can be altered by environmental exposures such as air pollution, individual behaviors, and social context, further investigation of these variations may reveal differences in PTB susceptibility. Such susceptibility may have resisted identification by studies that have simply examined exposures or genes alone, due to the lack of precision and accuracy of measurements and to unmeasured interactions between and within domains of exposure[127] indicated that studying epigenetic phenomena analytically can be informative for both in utero and transgenerational effects. Thus, it is known that epigenetic changes may be heritable as well as potentially reversible — with the former offering a possible explanation for observations from large epidemiologic studies that women are at higher risk for PTBs if they themselves were born preterm[128] and with the latter construct of reversibility offers opportunities for future prevention strategies.

FUTURE DIRECTIONS

As the above narrative shows, numerous studies have examined the role of single environmental exposures in influencing PTB risk, but few studies attempt to account for the complexities of multiple exposures — the exposome. Pregnant women are exposed to numerous environmental chemicals, psychosocial stressors, and variations in social constructs associated with the communities in which they live. A better understanding of the complexities of multiple exposures will facilitate etiologic discovery as well as provide evidence for policies and public health interventions.[129] Stingone and colleagues have suggested that to facilitate these efforts will require an interdisciplinary approach employing epidemiology, data science, and biomarker-based data collection that will combine to identify proximal biologic factors for PTB risk. As an illustration, being a race other than White, of lower SES, and residing in geographic areas with higher indices of social vulnerability have been associated with higher risks of PTB.[130] The cumulative impacts and potential interactions between elevated exposures to chemical and psychosocial stressors need to be explored further given that we have limited understanding of the extent to which prenatal exposures to environmental exposures and psychosocial stress act, independently and jointly, to contribute to PTB.

Factors that further modify the risks of the exposome will be important to explore in the future. Such factors can clearly include variations associated with the structural genome, epigenome, social stressors, and dietary factors. With respect to dietary influences on risk,[131] Eaves and Fry in their accompanying editorial of the study by Borghese and colleagues[116] where manganese was observed to inversely modify (antagonize) preeclampsia risk, suggested that dietary supplements that are known to contribute to detoxification pathways might be explored for their risk lowering impact. PTB risk associated with blood lead levels has been observed to be higher in women who also had lower blood levels of vitamin D.[132] Another recent example derives from Zhang and colleagues[117] in their study of adverse pregnancy outcomes and gestational exposures to perfluoroalkyl and PFAS, where they observed associations with earlier gestational age at delivery only among women whose prenatal dietary folate intake or plasma folate concentration was in the lowest quartile range. Low folate levels along with low intakes of low vitamins A, C, and E and carotene have been observed to modify the risk downward for PTB among women exposed to PAHs.[119] As Jardel and colleagues[133] recently observed, such studies have revealed a complex interplay between gestational diet and gestational timing of exposure to a particular air pollutant, on PTB risk, and therefore require substantial study populations to be informative.

PTB does not have a simple nor likely single etiology. PTB is a complex phenomenon and not well understood as a singular condition being defined only by the arbitrary dichotomy of birth of less than 37 completed weeks of gestation (vs $\geq$37 weeks).[6] This classification has been argued to be too simplistic for etiologic studies owing to the heterogeneity that has been observed with this outcome.[134] Indeed, finer phenotypic classifications have been suggested based on gestational timing such as less than 28 weeks, extremely preterm; 28 to 31 weeks, very preterm; and 32 to 36 weeks, moderately preterm weeks gestation,[135] or by sPTB versus medically indicated PTB. A very large proportion of the research between PTB and ambient environment has not fully considered these finer phenotypic definitions. There are indeed opportunities for substantial improvement going forward.

There is a growing understanding that PTB and other reproductive events have their etiologic roots in complex genomic–environment interactions. Thus, a concomitant

consideration of biologic, genetic, behavioral, social, and our ambient environmental exposures as risk factors is fundamental to unraveling the complex etiologies of PTB.

DISCLOSURE

The authors have nothing to disclose.

Best Practices

What is the current practice for preterm birth?

There is no known best practice for the prevention for preterm birth.

What changes in current practice are likely to improve outcomes?

More studies on the complexities of exposures in the ambient environment will inform policy efforts to reduce potentially harmful exposures during pregnancy.

Bibliographic Sources

Stingone JA, Triantafillou S, Larsen A, et al. Interdisciplinary data science to advance environmental health research and improve birth outcomes. Environ Res 2021;197:111,019.

REFERENCES

1. Howson CP, Kinney MV, Lawn JE, editors. March of Dimes, PMNCH, Save the children, world health organization. Born too soon: the global action report on preterm birth. Geneva: World Health Organization; 2012.
2. Walani SR. Global burden of preterm birth. Int J Gynaecol Obstet 2020; 150(1):31–3.
3. Goldenberg RL, Culhane JF, Iams JD, et al. Epidemiology and causes of preterm birth. Lancet 2008;371(9606):75–84.
4. Frey HA, Klebanoff MA. The epidemiology, etiology, and costs of preterm birth. Semin Fetal Neonatal Med 2016;21(2):68–73.
5. Blondel B, Kogan MD, Alexander GR, et al. The impact of the increasing number of multiple births on the rates of preterm birth and low birthweight: an international study. Am J Publ Health 2002;92(8):1323–30.
6. Behrman R, Butler A. Institute of Medicine (US) Committee on Understanding Premature Birth and Assuring Healthy Outcomes. Preterm birth: causes, consequences, and prevention. Washington, DC: National Academies Press; 2007.
7. Braveman P, Dominguez TP, Burke W, et al. Explaining the Black-White disparity in preterm birth: a consensus statement from a multi-disciplinary scientific work group convened by the March of Dimes. Front Reprod Health 2021;3:684207.
8. Chantarat T, Van Riper DC, Hardeman RR. Multidimensional structural racism predicts birth outcomes for Black and White Minnesotans. Health Serv Res 2022;57(3):448–57.
9. Martin JA, Kung HC, Mathews TJ, et al. Annual summary of vital statistics: 2006. Pediatrics 2008;121(4):788–801.
10. Bailey ZD, Krieger N, Agenor M, et al. Structural racism and health inequities in the USA: evidence and interventions. Lancet 2017;389(10077):1453–63.
11. Clark R, Anderson NB, Clark VR, et al. Racism as a stressor for African Americans. A biopsychosocial model. Am Psychol 1999;54(10):805–16.
12. Howe CJ, Bailey ZD, Raifman JR, et al. Recommendations for using causal diagrams to study racial health disparities. Am J Epidemiol 2022;191(12):1981–9.

13. Murphy DJ. Epidemiology and environmental factors in preterm labour. Best Pract Res Clin Obstet Gynaecol 2007;21(5):773–89.
14. Shaw GM, Mayo JA, Eisenberg ML, et al. Male-to-female ratios, race/ethnicity, and spontaneous preterm birth among 11 million California infants. Am J Perinatol 2021;38(7):683–9.
15. Prasad M, Jones M. Medical complications of opioid use disorder in pregnancy. Semin Perinatol 2019;43(3):162–7.
16. Gorman MC, Orme KS, Nguyen NT, et al. Outcomes in pregnancies complicated by methamphetamine use. Am J Obstet Gynecol 2014;211(4):429 e1–e7.
17. Hayatbakhsh MR, Flenady VJ, Gibbons KS, et al. Birth outcomes associated with cannabis use before and during pregnancy. Pediatr Res 2012;71(2):215–9.
18. Kibret KT, Chojenta C, Gresham E, et al. Maternal dietary patterns and risk of adverse pregnancy (hypertensive disorders of pregnancy and gestational diabetes mellitus) and birth (preterm birth and low birth weight) outcomes: a systematic review and meta-analysis. Public Health Nutr 2018;22(3):1–15.
19. Best KP, Gomersall J, Makrides M. Prenatal nutritional strategies to reduce the risk of preterm birth. Ann Nutr Metab 2020;76(Suppl 3):31–9.
20. Cui Y, Liao M, Xu A, et al. Association of maternal pre-pregnancy dietary intake with adverse maternal and neonatal outcomes: a systematic review and meta-analysis of prospective studies. Crit Rev Food Sci Nutr 2023;63(19):3430–51.
21. Li B, Zhang X, Peng X, et al. Folic acid and risk of preterm birth: a meta-analysis. Front Neurosci 2019;13:1284.
22. Wu Y, Wang J, Wei Y, et al. Maternal exposure to endocrine disrupting chemicals (EDCs) and preterm birth: a systematic review, meta-analysis, and meta-regression analysis. Environ Pollut 2022;292(Pt A):118264.
23. Dunlop AL, Kramer MR, Hogue CJ, et al. Racial disparities in preterm birth: an overview of the potential role of nutrient deficiencies. Acta Obstet Gynecol Scand 2011;90(12):1332–41.
24. Kramer MS, Kahn SR, Platt RW, et al. Antioxidant vitamins, long-chain fatty acids, and spontaneous preterm birth. Epidemiology 2009;20(5):707–13.
25. Myhre R, Brantsaeter AL, Myking S, et al. Intake of probiotic food and risk of spontaneous preterm delivery. Am J Clin Nutr 2011;93(1):151–7.
26. Cnattingius S, Villamor E, Johansson S, et al. Maternal obesity and risk of preterm delivery. JAMA 2013;309(22):2362–70.
27. Mayo JA, Stevenson DK, Shaw GM. Population-based associations between maternal pre-pregnancy body mass index and spontaneous and medically indicated preterm birth using restricted cubic splines in California. Ann Epidemiol 2022;72:65–73.
28. Shaw GM, Wise PH, Mayo J, et al. Maternal prepregnancy body mass index and risk of spontaneous preterm birth. Paediatr Perinat Epidemiol 2014;28(4):302–11.
29. Chu SY, Kim SY, Lau J, et al. Maternal obesity and risk of stillbirth: a metaanalysis. Am J Obstet Gynecol 2007;197(3):223–8.
30. Liang R, Panelli DM, Stevenson DK, et al. Associations between pregnancy glucose measurements and risk of preterm birth: a retrospective cohort study of commercially insured women in the United States from 2003 to 2021. Ann Epidemiol 2023;81:31–39 e19.
31. Marinovich ML, Regan AK, Gissler M, et al. Associations between interpregnancy interval and preterm birth by previous preterm birth status in four high-income countries: a cohort study. BJOG 2021;128(7):1134–43.

32. Shachar BZ, Mayo JA, Lyell DJ, et al. Interpregnancy interval after live birth or pregnancy termination and estimated risk of preterm birth: a retrospective cohort study. BJOG 2016;123(12):2009–17.
33. Tessema GA, Marinovich ML, Haberg SE, et al. Interpregnancy intervals and adverse birth outcomes in high-income countries: an international cohort study. PLoS One 2021;16(7):e0255000.
34. Lonhart JA, Mayo JA, Padula AM, et al. Short interpregnancy interval as a risk factor for preterm birth in non-Hispanic Black and White women in California. J Perinatol 2019;39(9):1175–81.
35. Klebanoff MA. Interpregnancy interval and pregnancy outcomes: causal or not? Obstet Gynecol 2017;129(3):405–7.
36. Tanigawa K, Ikehara S, Cui M, et al. Association between interpregnancy interval and risk of preterm birth and its modification by folate intake: the Japan Environment and Children's Study. J Epidemiol 2023;33(3):113–9.
37. Costello EK, DiGiulio DB, Robaczewska A, et al. Abrupt perturbation and delayed recovery of the vaginal ecosystem following childbirth. Nat Commun 2023;14(1):4141.
38. Dunkel Schetter C. Psychological science on pregnancy: stress processes, biopsychosocial models, and emerging research issues. Annu Rev Psychol 2011;62:531–58.
39. Holzman C, Senagore P, Tian Y, et al. Maternal catecholamine levels in midpregnancy and risk of preterm delivery. Am J Epidemiol 2009;170(8):1014–24.
40. Kramer MS, Lydon J, Seguin L, et al. Stress pathways to spontaneous preterm birth: the role of stressors, psychological distress, and stress hormones. Am J Epidemiol 2009;169(11):1319–26.
41. Becker M, Mayo JA, Phogat NK, et al. Deleterious and protective psychosocial and stress-related factors predict risk of spontaneous preterm birth. Am J Perinatol 2023;40(1):74–88.
42. Corchero-Falcon MDR, Gomez-Salgado J, Garcia-Iglesias JJ, et al. Risk factors for working pregnant women and potential adverse consequences of exposure: a systematic review. Int J Public Health 2023;68:1605655.
43. Ghosh R, Causey K, Burkart K, et al. Ambient and household PM2.5 pollution and adverse perinatal outcomes: a meta-regression and analysis of attributable global burden for 204 countries and territories. PLoS Med 2021;18(9):e1003718.
44. Bekkar B, Pacheco S, Basu R, et al. Association of air pollution and heat exposure with preterm birth, low birth weight, and stillbirth in the US: a systematic review. JAMA Netw Open 2020;3(6):e208243.
45. Liu XX, Fan SJ, Luo YN, et al. Global, regional, and national burden of preterm birth attributable to ambient and household PM(2.5) from 1990 to 2019: worsening or improving? Sci Total Environ 2023;871:161975.
46. Padula AM, Noth EM, Hammond SK, et al. Exposure to airborne polycyclic aromatic hydrocarbons during pregnancy and risk of preterm birth. Environ Res 2014;135:221–6.
47. Mekonnen A, Alemnew W, Abebe Z, et al. Adherence to iron with folic acid supplementation among pregnant women attending antenatal care in public health centers in Simada District, Northwest Ethiopia: using health belief model perspective. Patient Prefer Adherence 2021;15:843–51.
48. Amjad S, Chojecki D, Osornio-Vargas A, et al. Wildfire exposure during pregnancy and the risk of adverse birth outcomes: a systematic review. Environ Int 2021;156:106644.

49. Abdo M, Ward I, O'Dell K, et al. Impact of wildfire smoke on adverse pregnancy outcomes in Colorado, 2007-2015. Int J Environ Res Publ Health 2019;16(19):3720.
50. Heft-Neal S, Driscoll A, Yang W, et al. Associations between wildfire smoke exposure during pregnancy and risk of preterm birth in California. Environ Res 2022;203:111872.
51. Requia WJ, Kill E, Papatheodorou S, et al. Prenatal exposure to wildfire-related air pollution and birth defects in Brazil. J Expo Sci Environ Epidemiol 2022;32(4):596–603.
52. O'Donnell MH, Behie AM. Effects of wildfire disaster exposure on male birth weight in an Australian population. Evol Med Public Health 2015;2015(1):344–54.
53. Verstraeten BSE, Elgbeili G, Hyde A, et al. Maternal mental health after a wildfire: effects of social support in the Fort McMurray Wood Buffalo Study. Can J Psychiatr 2021;66(8):710–8.
54. Weber KA, Yang W, Carmichael SL, et al. Assessing associations between residential proximity to greenspace and birth defects in the National Birth Defects Prevention Study. Environ Res 2023;216(Pt 3):114760.
55. Cusack L, Larkin A, Carozza S, et al. Associations between residential greenness and birth outcomes across Texas. Environ Res 2017;152:88–95.
56. Sun Y, Sheridan P, Laurent O, et al. Associations between green space and preterm birth: windows of susceptibility and interaction with air pollution. Environ Int 2020;142:105804.
57. Laurent O, Wu J, Li L, et al. Green spaces and pregnancy outcomes in Southern California. Health Place 2013;24:190–5.
58. Glazer KB, Eliot MN, Danilack VA, et al. Residential green space and birth outcomes in a coastal setting. Environ Res 2018;163:97–107.
59. Casey JA, James P, Rudolph KE, et al. Greenness and birth outcomes in a range of Pennsylvania communities. Int J Environ Res Publ Health 2016;13(3):311.
60. Hystad P, Davies HW, Frank L, et al. Residential greenness and birth outcomes: evaluating the influence of spatially correlated built-environment factors. Environ Health Perspect 2014;122(10):1095–102.
61. Dalugoda Y, Kuppa J, Phung H, et al. Effect of elevated ambient temperature on maternal, foetal, and neonatal outcomes: a scoping review. Int J Environ Res Publ Health 2022;19(3):1771.
62. Son JY, Choi HM, Miranda ML, et al. Exposure to heat during pregnancy and preterm birth in North Carolina: main effect and disparities by residential greenness, urbanicity, and socioeconomic status. Environ Res 2022;204(Pt C):112315.
63. Wang Q, Yin L, Wu H, et al. Effects of gestational ambient extreme temperature exposures on the risk of preterm birth in China: a sibling-matched study based on a multi-center prospective cohort. Sci Total Environ 2023;887:164135.
64. Czolowski ED, Santoro RL, Srebotnjak T, et al. Toward consistent methodology to quantify populations in proximity to oil and gas development: a National Spatial Analysis and Review. Environ Health Perspect 2017;125(8):086004.
65. Cushing LJ, Vavra-Musser K, Chau K, et al. Flaring from unconventional oil and gas development and birth outcomes in the Eagle Ford Shale in South Texas. Environ Health Perspect 2020;128(7):77003.

66. Erickson CL, Barron IG, Zapata I. The effects of hydraulic fracturing activities on birth outcomes are evident in a non-individualized county-wide aggregate data sample from Colorado. J Public Health Res 2021;11(1):2551.
67. Gonzalez DJX, Sherris AR, Yang W, et al. Oil and gas production and spontaneous preterm birth in the San Joaquin Valley, CA: a case-control study. Environ Epidemiol 2020;4(4):e099.
68. Hill EL. Shale gas development and infant health: evidence from Pennsylvania. J Health Econ 2018;61:134–50.
69. McKenzie LM, Guo R, Witter RZ, et al. Birth outcomes and maternal residential proximity to natural gas development in rural Colorado. Environ Health Perspect 2014;122(4):412–7.
70. Tran KV, Casey JA, Cushing LJ, et al. Residential proximity to oil and gas development and birth outcomes in California: a retrospective cohort study of 2006-2015 births. Environ Health Perspect 2020;128(6):67001.
71. Tran KV, Casey JA, Cushing LJ, et al. Residential proximity to hydraulically fractured oil and gas wells and adverse birth outcomes in urban and rural communities in California (2006-2015). Environ Epidemiol 2021;5(6):e172.
72. Walker Whitworth K, Kaye Marshall A, Symanski E. Drilling and production activity related to unconventional gas development and severity of preterm birth. Environ Health Perspect 2018;126(3):037006.
73. Whitworth KW, Marshall AK, Symanski E. Maternal residential proximity to unconventional gas development and perinatal outcomes among a diverse urban population in Texas. PLoS One 2017;12(7):e0180966.
74. Stacy SL, Brink LL, Larkin JC, et al. Perinatal outcomes and unconventional natural gas operations in Southwest Pennsylvania. PLoS One 2015;10(6):e0126425.
75. Adgate JL, Goldstein BD, McKenzie LM. Potential public health hazards, exposures and health effects from unconventional natural gas development. Environ Sci Technol 2014;48(15):8307–20.
76. Gonzalez DJX, Francis CK, Shaw GM, et al. Upstream oil and gas production and ambient air pollution in California. Sci Total Environ 2022;806(Pt 1):150298.
77. Deziel NC, Clark CJ, Casey JA, et al. Assessing exposure to unconventional oil and gas development: strengths, challenges, and implications for epidemiologic research. Curr Environ Health Rep 2022;9(3):436–50.
78. Cairncross ZF, Couloigner I, Ryan MC, et al. Association between residential proximity to hydraulic fracturing sites and adverse birth outcomes. JAMA Pediatr 2022;176(6):585–92.
79. Caron-Beaudoin E, Whyte KP, Bouchard MF, et al. Volatile organic compounds (VOCs) in indoor air and tap water samples in residences of pregnant women living in an area of unconventional natural gas operations: findings from the EXPERIVA study. Sci Total Environ 2022;805:150242.
80. Shepherd TH. Catalog of teratogenic agents (Shepherd's Catalog) last updated through Micromedex 2009. 8th edition. Baltimore: John Hopkins University Press; 1995.
81. Acosta-Maldonado B, Sanchez-Ramirez B, Reza-Lopez S, et al. Effects of exposure to pesticides during pregnancy on placental maturity and weight of newborns: a cross-sectional pilot study in women from the Chihuahua State, Mexico. Hum Exp Toxicol 2009;28(8):451–9.
82. Pathak R, Suke SG, Ahmed T, et al. Organochlorine pesticide residue levels and oxidative stress in preterm delivery cases. Hum Exp Toxicol 2010;29(5):351–8.

83. Windham GC, Lee D, Mitchell P, et al. Exposure to organochlorine compounds and effects on ovarian function. Epidemiology 2005;16(2):182–90.
84. Wigle DT, Arbuckle TE, Turner MC, et al. Epidemiologic evidence of relationships between reproductive and child health outcomes and environmental chemical contaminants. J Toxicol Environ Health B Crit Rev 2008;11(5–6):373–517.
85. Shirangi A, Nieuwenhuijsen M, Vienneau D, et al. Living near agricultural pesticide applications and the risk of adverse reproductive outcomes: a review of the literature. Paediatr Perinat Epidemiol 2011;25(2):172–91.
86. Rinsky JL, Hopenhayn C, Golla V, et al. Atrazine exposure in public drinking water and preterm birth. Publ Health Rep 2012;127(1):72–80.
87. Harley KG, Huen K, Aguilar Schall R, et al. Association of organophosphate pesticide exposure and paraoxonase with birth outcome in Mexican-American women. PLoS One 2011;6(8):e23923.
88. Stillerman KP, Mattison DR, Giudice LC, et al. Environmental exposures and adverse pregnancy outcomes: a review of the science. Reprod Sci 2008;15(7):631–50.
89. Willis WO, de Peyster A, Molgaard CA, et al. Pregnancy outcome among women exposed to pesticides through work or residence in an agricultural area. J Occup Med 1993;35(9):943–9.
90. Longnecker MP, Klebanoff MA, Zhou H, et al. Association between maternal serum concentration of the DDT metabolite DDE and preterm and small-for-gestational-age babies at birth. Lancet 2001;358(9276):110–4.
91. Kadhel P, Monfort C, Costet N, et al. Chlordecone exposure, length of gestation, and risk of preterm birth. Am J Epidemiol 2014;179(5):536–44.
92. Winchester P, Proctor C, Ying J. County-level pesticide use and risk of shortened gestation and preterm birth. Acta Paediatr 2016;105(3):e107–15.
93. Shaw GM, Yang W, Roberts EM, et al. Residential agricultural pesticide exposures and risks of spontaneous preterm birth. Epidemiology 2018;29(1):8–21.
94. Shaw GM, Yang W, Roberts EM, et al. Residential agricultural pesticide exposures and risks of preeclampsia. Environ Res 2018;164:546–55.
95. Ferguson KK, Chin HB. Environmental chemicals and preterm birth: biological mechanisms and the state of the science. Curr Epidemiol Rep 2017;4(1):56–71.
96. Currie J, Zivin JG, Meckel K, et al. Something in the water: contaminated drinking water and infant health. Can J Econ 2013;46(3):791–810.
97. Sharma S, Bhattacharya AJ. Drinking water contamination and treatment techniques. Appl Water Sci 2017;7(3):1043–67.
98. Capdeville MJ, Budzinski H. Trace-level analysis of organic contaminants in drinking waters and groundwaters. TrAC, Trends Anal Chem 2011;30(4):586–606.
99. Ochoa-Acuna H, Frankenberger J, Hahn L, et al. Drinking-water herbicide exposure in Indiana and prevalence of small-for-gestational-age and preterm delivery. Environ Health Perspect 2009;117(10):1619–24.
100. Kumar S, Forand S, Babcock G, et al. Total trihalomethanes in public drinking water supply and birth outcomes: a cross-sectional study. Matern Child Health J 2014;18(4):996–1006.
101. Tardiff RG, Carson ML, Ginevan ME. Updated weight of evidence for an association between adverse reproductive and developmental effects and exposure to disinfection by-products. Regul Toxicol Pharmacol 2006;45(2):185–205.

102. Huang H, Woodruff TJ, Baer RJ, et al. Investigation of association between environmental and socioeconomic factors and preterm birth in California. Environ Int 2018;121(Pt 2):1066–78.
103. Lin L, St Clair S, Gamble GD, et al. Nitrate contamination in drinking water and adverse reproductive and birth outcomes: a systematic review and meta-analysis. Sci Rep 2023;13(1):563.
104. Young HA, Kolivras KN, Krometis LH, et al. Examining the association between safe drinking water act violations and adverse birth outcomes in Virginia. Environ Res 2023;218:114977.
105. Sherris AR, Baiocchi M, Fendorf S, et al. Nitrate in drinking water during pregnancy and spontaneous preterm birth: a retrospective within-mother analysis in California. Environ Health Perspect 2021;129(5):57001.
106. Coffman VR, Jensen AS, Trabjerg BB, et al. Prenatal exposure to nitrate from drinking water and markers of fetal growth restriction: a population-based study of nearly one million Danish-born children. Environ Health Perspect 2021;129(2):27002.
107. Padula AM, Huang H, Baer RJ, et al. Environmental pollution and social factors as contributors to preterm birth in Fresno County. Environ Health 2018;17(1):70.
108. Lin MC, Chiu HF, Yu HS, et al. Increased risk of preterm delivery in areas with air pollution from a petroleum refinery plant in Taiwan. J Toxicol Environ Health 2001;64(8):637–44.
109. Tsai SS, Yu HS, Liu CC, et al. Increased incidence of preterm delivery in mothers residing in an industrialized area in Taiwan. J Toxicol Environ Health 2003;66(11):987–94.
110. Yang CY, Chang CC, Tsai SS, et al. Preterm delivery among people living around Portland cement plants. Environ Res 2003;92(1):64–8.
111. Tsai SS, Yu HS, Chang CC, et al. Increased risk of preterm delivery in women residing near thermal power plants in Taiwan. Arch Environ Health 2004;59(9):478–83.
112. Mendrinos A, Ramesh B, Ruktanonchai CW, et al. Poultry concentrated animal-feeding operations on the Eastern Shore, Virginia, and geospatial associations with adverse birth outcomes. Healthcare (Basel) 2022;10(10):2016.
113. Wing SE, Larson TV, Hudda N, et al. Aircraft noise and vehicle traffic-related air pollution interact to affect preterm birth risk in Los Angeles, California. Sci Total Environ 2022;829:154678.
114. Sun J, Yang R, Xian H, et al. Association between maternal family history of hypertension and preterm birth: modification by noise exposure and multivitamin intake. J Matern Fetal Neonatal Med 2022;35(26):10458–65.
115. Basner M, Babisch W, Davis A, et al. Auditory and non-auditory effects of noise on health. Lancet 2014;383(9925):1325–32.
116. Borghese MM, Fisher M, Ashley-Martin J, et al. Individual, independent, and joint associations of toxic metals and manganese on hypertensive disorders of pregnancy: results from the MIREC Canadian pregnancy cohort. Environ Health Perspect 2023;131(4):47014.
117. Zhang Y, Mustieles V, Sun Q, et al. Association of early pregnancy perfluoroalkyl and polyfluoroalkyl substance exposure with birth outcomes. JAMA Netw Open 2023;6(5):e2314934.
118. Meng Q, Inoue K, Ritz B, et al. Prenatal exposure to perfluoroalkyl substances and birth outcomes; an updated analysis from the Danish National Birth Cohort. Int J Environ Res Publ Health 2018;15(9):1832.

119. Zhao N, Wu W, Cui S, et al. Effects of benzo[a]pyrene-DNA adducts, dietary vitamins, folate, and carotene intakes on preterm birth: a nested case-control study from the birth cohort in China. Environ Health 2022;21(1):48.
120. Chin HB, Jukic AM, Wilcox AJ, et al. Association of urinary concentrations of early pregnancy phthalate metabolites and bisphenol A with length of gestation. Environ Health 2019;18(1):80.
121. Zhang Y, Mustieles V, Williams PL, et al. Parental preconception exposure to phenol and phthalate mixtures and the risk of preterm birth. Environ Int 2021; 151:106440.
122. Jain VG, Monangi N, Zhang G, et al. Genetics, epigenetics, and transcriptomics of preterm birth. Am J Reprod Immunol 2022;88(4):e13600.
123. Surkan PJ, Hong X, Zhang B, et al. Can social support during pregnancy affect maternal DNA methylation? Findings from a cohort of African-Americans. Pediatr Res 2020;88(1):131–8.
124. Xu R, Hong X, Zhang B, et al. DNA methylation mediates the effect of maternal smoking on offspring birthweight: a birth cohort study of multi-ethnic US mother-newborn pairs. Clin Epigenet 2021;13(1):47.
125. Ladd-Acosta C, Feinberg JI, Brown SC, et al. Epigenetic marks of prenatal air pollution exposure found in multiple tissues relevant for child health. Environ Int 2019;126:363–76.
126. Park B, Khanam R, Vinayachandran V, et al. Epigenetic biomarkers and preterm birth. Environ Epigenet 2020;6(1):dvaa005.
127. Saenen ND, Martens DS, Neven KY, et al. Air pollution-induced placental alterations: an interplay of oxidative stress, epigenetics, and the aging phenotype? Clin Epigenet 2019;11(1):124.
128. Klebanoff MA, Schulsinger C, Mednick BR, et al. Preterm and small-for-gestational-age birth across generations. Am J Obstet Gynecol 1997;176(3): 521–6.
129. Stingone JA, Triantafillou S, Larsen A, et al. Interdisciplinary data science to advance environmental health research and improve birth outcomes. Environ Res 2021;197:111019.
130. Givens M, Teal EN, Patel V, et al. Preterm birth among pregnant women living in areas with high social vulnerability. Am J Obstet Gynecol MFM 2021;3(5): 100414.
131. Eaves LA, Fry RC. Invited perspective: toxic metals and hypertensive disorders of pregnancy. Environ Health Perspect 2023;131(4):41303.
132. Fisher M, Marro L, Arbuckle TE, et al. Association between toxic metals, vitamin D and preterm birth in the maternal-infant research on environmental chemicals study. Paediatr Perinat Epidemiol 2023;37(5):447–57.
133. Jardel H, Martin CL, Hoyo C, et al. Interplay of gestational parent exposure to ambient air pollution and diet characteristics on preterm birth. BMC Publ Health 2023;23(1):822.
134. Zhang J, Savitz DA. Duration of Gestation and Timing of Birth. New York: Oxford University Press; 2011.
135. McElrath TF, Hecht JL, Dammann O, et al. Pregnancy disorders that lead to delivery before the 28th week of gestation: an epidemiologic approach to classification. Am J Epidemiol 2008;168(9):980–9.