Invited Commentary

Invited Commentary: Ambient Environment and the Risk of Preterm Birth

Sandie Ha and Pauline Mendola*

* Correspondence to Dr. Pauline Mendola, Epidemiology Branch, Division of Intramural Population Health Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development, 6710B Rockledge Drive Room 3119, Bethesda, MD 20817 (e-mail: pauline.mendola@nih.gov).

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Preterm birth is a common adverse birth outcome known to be associated with increased infant mortality, and it often results in a higher burden of offspring morbidity in both the short and long terms. The potential for environmental factors, particularly air pollution and meteorological parameters, to increase preterm birth risk has received significant attention worldwide, but the findings are generally inconsistent, with variations in study designs and methods across populations and geographic locations. In the current issue of the Journal, Giorgis-Allemand et al. (Am J Epidemiol. 2017;185(4):247–258) take the field a step further than most prior investigations of the ambient environment. They examined the associations of ambient air pollution and meteorological factors with preterm risk among 13 cohorts across 11 European countries. No association with air pollution was observed, but associations with increased preterm birth risk were found for both increased atmospheric pressure and ambient temperature exposures during the first trimester. The study is notable in attempting to address several important issues that challenge the field, including exposure misclassification and defining critical windows of exposure. Their comprehensive evaluation of ambient exposures is to be commended.

Abbreviation: PM, particulate matter.

Preterm birth (birth occurring before 37 weeks of gestation) is a common adverse birth outcome worldwide, with increasing trends in most countries with reliable data (1). Preterm infants have a significantly increased risk of mortality and serious health problems, including lifelong developmental complications (2). Environmental factors that could contribute to preterm birth risk have received increasing attention in the literature. Specifically, there is growing interest in the effects of prenatal exposures to extreme ambient temperature and air pollution on preterm birth risk (3, 4), given the increasing global concerns related to climate change and pollution emissions from anthropogenic sources (5). Even with this increased attention, no consistent pattern of results has emerged, perhaps due to heterogeneity in study populations, exposure, and outcome assessments, as well as variation in other study design attributes. Moving beyond temperature and humidity to other meteorological exposures, such as atmospheric pressure, is an interesting development that does not seem to have been studied previously in relation to preterm birth risk (6). The accompanying study by Giorgis-Allemand et al. (7) is the first large, international study to simultaneously examine the associations of air pollution and various meteorological factors with preterm birth risk in a generally temperate area. These authors take advantage of a large, pooled data set consisting of 3,533 preterm births among 71,493 singleton births (5%) from 13 cohorts across 11 European countries from 1994–2010. In general, while the authors observed no association with air pollution, they found associations with increased atmospheric pressure (that could not be distinguished from altitude) and ambient temperature exposures during the first trimester. The study is notable in attempting to address several important issues that challenge the field, including exposure misclassification and defining critical windows of exposure. Their comprehensive evaluation of ambient exposures is to be commended.
with aerodynamic diameter less than or equal to 2.5 μm or 10 μm (PM$_{2.5}$ or PM$_{10}$), coarse PM (PM$_{2.5-10}$), PM$_{1.5}$ absorbance, nitrogen dioxide, and nitrogen oxides were assessed at maternal home addresses using outputs from land-use regression models. The use of this model is popular in the literature because it can temporally and spatially estimate various pollution exposures based on data from monitor stations. However, it has limitations (8). For example, it does not include other meteorological inputs such as wind direction and speed, which could affect air pollution levels. Other exposure models may be more computationally intensive but also more flexible, including the Community Multi-scale Air Quality (9, 10) or hierarchical Bayesian models (11), which allow inputs from a variety of sources, including emissions data, observed measures at local monitoring stations, and meteorology, and can consider atmospheric mixing and the interaction of the photochemical properties of air pollutants.

Most studies of ambient environmental exposures and preterm birth are based on estimates for the residential address at delivery and are unable to adjust for residential history or daily activity patterns, leading to potential exposure misclassification. Despite the lack of data on daily activities (use of air conditioners or heaters, time spent indoors, or time spent at work or in other locations outside the home, etc.), the present study makes an important advancement by 1) using a time-weighted average of exposure at all addresses for participants who had that information available (15% of participants in 11 cohorts) and 2) performing a sensitivity analysis restricted to women who had not relocated. The authors reported that their sensitivity analysis showed that the lack of residential history did not induce a strong bias, which is consistent with another study on this topic (12). However, exposure misclassification at some level is inevitable, given that up to 30% of pregnant women may relocate during the course of pregnancy (13) and that a residential exposure essentially assumes that women stay stationary at their residential address (outdoors) throughout the day (obviously unrealistic) or that the variation in actual exposure that is bound to occur with local mobility and indoor/outdoor gradients is not likely to change effect estimates in an important way. Adjustments for residential history and daily activity patterns remain important challenges for the field to overcome moving forward, but the steps made by Giorgis-Allemand et al. are an improvement.

Another challenge we face is identifying and understanding the critical window of exposure for preterm birth risk, if indeed there is one. In this study, exposures were assessed over several potentially critical windows: trimester 1; trimester 2; and 1-week, 4-week, and whole-pregnancy windows, excluding exposures after 37 weeks. This method allowed the authors to assess the potential impact of early-pregnancy, chronic, and acute (previous week and previous month) exposures. For the previous week and month exposures, the authors used survival models to estimate the risk of preterm birth. The breadth of windows covered is comprehensive, and the authors have tried to identify key windows of exposure associated with risk. The approach appears to work well for the more chronic windows, but triggering or acute effects of environmental hazards with transient exposures may be better assessed using a case-crossover analysis, which additionally allows adjustment for time-invariant confounders (14).

In their analyses, the authors included study site as a random effect with the intent to control for variation in area-level differences between the sites. This is a difficult decision, given that it will also take away some of the variation in exposure that may relate to risk differences across sites. Their site-specific analyses did show risk differences across sites, suggesting that the relationship between preterm birth and both meteorological and pollution effects may be differential across geographic areas and may need more investigation. This may be related to women’s ability to acclimate to their usual environment, differences in the composition of particles based on local sources, lower precision due to smaller samples, or other unmeasured factors. Because of the control for study site, we expect that the findings here were conservative.

The prevalence of preterm delivery in the study is 5%, which, as the authors noted, is relatively low compared to many parts of the world. This may have limited the study’s power for some subanalyses. We note that the authors were able to demonstrate consistent results when excluding those who had (or had planned to have) a cesarean delivery; however, it is also important to note that indicated preterm deliveries may still be among the restricted sample because, presumably, some women will deliver vaginally after induction. Whether those medically indicated deliveries could also be related in part to ambient exposure is another issue for consideration, given that hypertensive disorders of pregnancy are a common indication for early delivery, and those disorders may be related to air pollution (15). The use of a standard cutoff to define preterm delivery at 37 weeks is sensible, but because there is evidence that early term births (37–38 weeks) are subject to higher health burden compared to full-term births (≥39 weeks), those deliveries at early term may need more attention in this field (16).

Last, we commend the authors for their transparency in displaying the multiple ways they addressed this important problem. Their approach, examining a suite of ambient exposures in a comprehensive manner, is refreshing and reminds us all that there are complex interrelationships between pollutants, temperature, and other meteorological factors that exist in combination in the real world. We can do a better job of modeling that real world to estimate risks more appropriately, and Giorgis-Allemand et al. have provided us with a good example here.

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Author affiliations: Epidemiology Branch, Division of Intramural Population Health Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda, Maryland (Sandie Ha, Pauline Mendola).

All authors contributed equally to this work.

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