American Journal of Epidemiology

Vol. 185, No. 4
DOI: 10.1093/aje/kww142
Advance Access publication:
January 13, 2017

Response to Invited Commentary

Giorgis-Allemand et al. Respond to “Ambient Environment and Preterm Birth”

Lise Giorgis-Allemand, Marie Pedersen, Rob M. J. Beelen, Ulrike Gehring, Gerard Hoek, Xavier Basagana, Mark J. Nieuwenhuijsen, Bert Brunekreef, Manolis Kogevinas, and Rémy Slama*

* Correspondence to Dr. Rémy Slama, Team of Environmental Epidemiology, INSERM/Centre National de la Recherche Scientifique (CNRS)/Université Grenoble Alpes Joint Research Center (Insitute for Advanced Biosciences, U1209), Allée des Alpes, 38700 La Tronche, France (e-mail: remy.slama@univ-grenoble-alpes.fr).

Initially submitted September 22, 2016; accepted for publication October 20, 2016.

We thank Drs. Ha and Mendola for their thoughtful comments (1) on our study of associations of meteorological conditions and air pollution levels with preterm birth risk (2).

Over the last decade, the spatial resolution of exposure models for atmospheric pollution has improved. Ha and Mendola mention, among other models, dispersion models as possibly more relevant alternatives to the land-use regression (LUR) approach used in the European Study of Cohorts for Air Pollution Effects (ESCAPE), in which our study was embedded. It should be noted that, although not explicitly considered by LUR models, meteorological conditions are still indirectly taken into account through their influence on local air pollution levels, which constitute an entry parameter of our seasonalized LUR model (2, 3). A detailed comparison of the yearly estimates of our LUR model and of dispersion models at home addresses, made in the European Study of Cohorts for Air Pollution Effects, showed a median (Pearson’s *r*) correlation of 0.75 for nitrogen dioxide and 0.29 for fine particulate matter, with stronger agreement in areas where dispersion models were more predictive of the local measurements done to define LUR models (4). These models should not be opposed, and estimates from dispersion models and other models can actually be fed into LUR models to increase their predictive ability (5).

Further improving the spatial resolution of models below the 10-m to 100-m values of typical current models is unlikely to significantly improve accuracy in exposure estimates as long as the time-space activity of pregnant women is not considered (6). In a small-scale study of pregnant women carrying Global Positioning System devices in a mid-size French city, incorporating time-space activity in an exposure estimate based on an (outdoor) dispersion model produced little change in exposure estimates for fine particulate matter (a pollutant with limited spatial variability within urban areas) and somewhat larger but still limited changes for nitrogen dioxide exposure estimates (7). More generally, it has been shown that bias in dose-response functions due to ignoring time-space activity is likely to increase as spatial resolution of exposure models becomes finer (6).

Taking indoor air pollution levels into account seemed to have a greater impact on exposure estimates (7), which is coherent with the limited correlation reported between personal and outdoor exposures outside the context of pregnancy (8). However, dosimeters cannot easily be carried for more than a few weeks during a pregnancy, thus offering a better consideration of indoor levels at the cost of a decreased ability to test numerous exposure windows during the pregnancy. Modeling indoor infiltration of outdoor pollutants could be a way to better take indoor levels into account without decreasing the temporal resolution of exposure estimates (9).

Considering larger areas is an option for increasing the sample size. As Ha and Mendola rightly pointed out (1), there is no consensus as to the best way to correct for bias possibly resulting from the consideration of large study areas (10). The main concern here relates to confounding bias. In the context of a birth cohort, Pedersen et al. (10) showed that as the area considered around the city centers was extended, thus increasing sample size, the heterogeneity of the population increased in terms of disease risk factors, thus increasing the potential for bias in a situation where all confounders cannot be perfectly measured; this is but an illustration of the well-known bias-variance tradeoff. We chose to adjust for the study area using a random-effect covariate (2). In the case of associations with first-trimester atmospheric pressure, not adjusting for study center at all did not yield an increased point estimate (odds ratio per 5-mBar increase = 1.04, compared with 1.06 after controlling for study center with a random-effect variable) (2); taking the study center into account might indeed lead to overadjustment, but it can reduce confounding bias due to variations between locations in the risk factors for preterm birth. Alternatives exist (11), and further work is needed to identify the least biased approach to take the study center and, more generally, unmeasured spatially varying confounders into account.

We considered preterm (before 37 gestational weeks) and very preterm (before 32 completed gestational weeks) births. As Ha and Mendola suggested, we have conducted an analysis of the risk of early term birth (births occurring at 37–38 weeks, using births taking place at ≥39 weeks as the reference group). These analyses indicated a monotonic association between the risk of early term birth and temperature averaged until week 37 (odds ratio = 1.24 per 10°C increase, 95% confidence interval: 1.06, 1.46) and no association with first-trimester average atmospheric pressure ($P = 0.53$)—a different pattern from that observed for preterm birth risk (2). Discerning preterm birth cases according to the underlying maternal, placental, or fetal conditions would be another relevant step in the future.

Our study provided an illustration of bias that can arise when analyzing associations of preterm birth risk with exposures during a time window spanning until birth, as is the case of exposures during the third trimester of pregnancy. When associations with this exposure window were estimated using a statistical model that did not accommodate time-varying exposures, such as logistic regression, a clear bias was highlighted for temperature, compared with estimates using a survival analysis (2). Such a bias may occur for other time-varying exposures, such as exposure to atmospheric pollutants. A meta-analysis indicated that there was no overall evidence for variations in preterm birth risk with particulate-matter levels assessed in either the first or second trimesters of pregnancy (12). The meta-analysis was in support of a detrimental association only for the third-trimester and whole-pregnancy exposure windows (12). These are precisely the exposure windows for which the potential exists for the bias related to exposures of term and preterm births being averaged over different durations when logistic regression is used, which seems to have been the case for most of these studies. For these reasons, we believe an important step to move the question forward would be for authors of past studies to repeat their analyses of third-trimester and whole-pregnancy exposure windows using a survival approach or any other approach that can reduce the potential for this bias to happen. This is likely to shed some light on the important but still dusky area of air pollution effects on preterm birth risk.

ACKNOWLEDGMENTS

Author affiliations: Team of Environmental Epidemiology Applied to Reproduction and Respiratory Health, Insitute for Advanced Biosciences, INSERM/Centre National de la Recherche Scientifique (CNRS)/Université Grenoble Alpes Joint Research Center, Grenoble, France (Lise Giorgis-Allemand, Marie Pedersen, Rémy Slama); Institute for Risk Assessment Sciences, Utrecht University, Utrecht, the Netherlands (Rob M. J. Beelen, Ulrike Gehring, Gerard Hoek, Bert Brunekreef); and ISGlobal Barcelona Institute for Global Health, Barcelona, Spain (Marie Pedersen, Xavier Basagana, Mark Nieuwenhuijsen, Manolis Kogevinas).

Conflict of interest: none declared.

REFERENCES

1. Ha S, Mendola P. Invited commentary: ambient environment and the risk of preterm birth. *Am J Epidemiol*. 2017;185(4):259–261.
2. Giorgis-Allemand L, Pedersen M, Bernard C, et al. The influence of meteorological factors and atmospheric pollutants on the risk of preterm birth. *Am J Epidemiol*. 2017;185(4):247–258.
3. Pedersen M, Giorgis-Allemand L, Bernard C, et al. Ambient air pollution and low birthweight: a European cohort study (ESCAPE). *Lancet Respir Med*. 2013;1(9):695–704.
4. de Hoogh K, Korek M, Vienneau D, et al. Comparing land use regression and dispersion modelling to assess residential exposure to ambient air pollution for epidemiological studies. *Environ Int*. 2014;73:382–392.
5. Korek M, Johansson C, Svensson N, et al. Can dispersion modeling of air pollution be improved by land-use regression? An example from Stockholm, Sweden [published online ahead of print August 3, 2016]. *J Expo Sci Environ Epidemiol*. (doi:10.1038/jes.2016.40).
6. Setton E, Marshall JD, Brauer M, et al. The impact of daily mobility on exposure to traffic-related air pollution and health effect estimates. *J Expo Sci Environ Epidemiol*. 2011;21(1):42–48.
7. Ouidir M, Giorgis-Allemand L, Lyon-Caen S, et al. Estimation of exposure to atmospheric pollutants during pregnancy integrating space-time activity and indoor air levels: does it make a difference? *Environ Int*. 2015;84:161–173.
8. Avery CL, Mills KT, Williams R, et al. Estimating error in using residential outdoor $PM_{2.5}$ concentrations as proxies for personal exposures: a meta-analysis. *Environ Health Perspect*. 2010;118(5):673–678.
9. Allen RW, Adar SD, Avol E, et al. Modeling the residential infiltration of outdoor $PM_{2.5}$ in the Multi-Ethnic Study of Atherosclerosis and Air Pollution (MESA Air). *Environ Health Perspect*. 2012;120(6):824–830.
10. Pedersen M, Siroux V, Pin I, et al. Does consideration of larger study areas yield more accurate estimates of air pollution health effects? An illustration of the bias-variance trade-off in air pollution epidemiology. *Environ Int*. 2013;60:23–30.
11. Jerrett M, Gale S, Kontgis C. Spatial modeling in environmental and public health research. *Int J Environ Res Public Health*. 2010;7(4):1302–1329.
12. Stieb DM, Chen L, Eshoul M, et al. Ambient air pollution, birth weight and preterm birth: a systematic review and meta-analysis. *Environ Res*. 2012;117:100–111.