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Airborne Particulate Matter and Acute Lung Inflammation

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In their article, Strak et al. (2012) connected real-world exposure to markers of acute lung function and inflammation. However, some points in the paper require further explanation. Strak et al. used fractional exhaled nitric oxide (FE_{NO}) as a marker of lung inflammation. Exhaled NO is produced throughout the respiratory tract and shows significant variability in source strength across the respiratory tract (Barnes et al. 2010; Kharitonov and Barnes 2001). Factors such as particle size, hygroscopicity, composition, and concentration; lung function parameters; and environmental temperature and humidity (Varghese and Gangamma 2006, 2009), which vary across experimental locations and between participants, modify particle deposition sites in the lung. These changes in the deposition site may influence the amount of NO exhaled. In their paper, Strak et al. (2012) did not discuss how these parameters influenced their conclusions. Thus, how the linear regression model they used accounts for these influences needs to be explained.

Inflammation in the lung resulting from air pollution exposure involves various cell types, such as epithelial cells in upper airways and macrophages and recruited neutrophils in the lower respiratory tract. A significant source of exhaled NO is epithelial cells in the upper airways, which are associated with eosinophilic inflammation (Barnes et al. 2010; Kharitonov and Barnes 2001). Many components of particulate matter (PM), such as endotoxin or bacteria, induce neutrophil inflammation in the lung, but the effects of these components may not be reflected in the concentration of exhaled NO. Thus, FE_{NO} measurements as a marker of inflammation could easily be misinterpreted by attributing a particular part of the total inflammatory response within the lung to air pollution. Strak et al. (2012) did not discuss such possibilities.

In their article, Strak et al. (2012) did not provide sufficient details about the NIOX MINO monitor (Aerocrine 2010) they used to measure exhaled NO concentration. I assume that NO measurement involves flow measurement and diffusion of NO to a sensor. Temperature and humidity of exhaled air or body temperature of the subjects likely interfere with these operations. Strak et al. did not describe any of these parameters or how they may interfere with NO measurement. Moreover, the absolute values of FE_{NO} observed during the experiments are not readily available. However, in the "Discussion," Strak et al. indicated that the observed variations between FE_{NO} measurements that are associated with particle number concentration (PNC) were most likely within the range of 5–15%. The technical specification of the instrument used for NO measurement has precision values of 5 ppb or 10% for concentrations > 30 ppb (Aerocrine 2010). Strak et al. used the difference between two sets of readings (preexposure and postexposure) as the input data for regression calculations. Thus, measurement error associated with the calculations could be much higher than that for a single set of measurements. Therefore, many of the observed differences in NO values were likely to fall within the error range of the instrument. Strak et al. should have discussed the propagation of error in the measurements or provided sufficient experimental data on the precision of the measurements. They should also have explained how the regression analysis is not biased by such instrument errors.

Strak et al. (2012) reported measurement of PNC with a condensation particle counter (CPC model 3007; TSI 2007), but their Table S2 did not report the accuracy or limit of detection of this instrument. CPC measurement depends on parameters such as ion concentration and particle composition, but because the measurements in the paper were from different environments, it is likely that these parameters varied significantly across the sites. Moreover, the CPC has a low sampling flow rate, and it is not clear whether this sampling rate is suitable for ambient measurement (aspiration efficiency in case of fluctuations in ambient wind velocity).

Overall, the article is an excellent attempt by Strak et al. (2012) to use noninvasive methods to understand the acute response of the respiratory system in response to air pollution exposure. However, a careful explanation of theory behind the experiments, experimental design, and limitations of measurement methods (if any) should have been discussed in the article.

The author declares he has no actual or potential competing financial interests

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Airborne Particulate Matter and Acute Lung Inflammation: Strak et al. Respond

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We thank Gangamma for a number of excellent observations and would like to respond to the issues raised.

Gangamma points out that the levels of fractional exhaled nitric oxide (FE_{NO}) may be influenced by the site of particle deposition in the lung and requests further explanation on how this could affect the analysis and conclusion of our study (Strak et al. 2012). In an observational study such as ours, it is not possible to assess precise locations of particle deposition in the respiratory tract. Although variations in location of particle deposition likely introduced some noise in the FE_{NO} readings, we could not take this into account in the regression model.

Gangamma notes that many components of particulate matter (PM) can induce neutrophil inflammation in the lung; thus, focusing only on FE_{NO} may not sufficiently reflect their effects. FE_{NO} is an indicator of airway inflammation that is used fairly often in observational and experimental studies. As we stated above, in a study such as ours (Strak et al. 2012), it would be very challenging to address many possible inflammation pathways. In addition, the focus of our study was more on the components and characteristics of air pollution and associated health effects. We included other inflammatory markers (e.g., interleukin-6, neutrophils) measured both in blood and nasal lavage in our health measurements, but those were outside of the scope of our paper.

The next issue raised by Gangamma deals with the suggestion that many of the measured FE_{NO} values could be within error range of the measurement instrument; therefore, data on the precision of the measurements should be provided and explanation should be given on how it could affect the regression analysis. Measurement error is an