Air pollution and traffic noise: do they cause atherosclerosis?

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This editorial refers to ‘Are air pollution and traffic noise independently associated with atherosclerosis: the Heinz Nixdorf Recall Study’¹, by H. Kälsch et al., on page 853

The great majority of the world’s population is continuously exposed to some level of air pollution from transportation, household sources, agriculture, and industry, and many are also exposed to ambient noise from the same sources. It has been estimated that globally ~ 3 million premature deaths are attributable to outdoor air pollution each year,¹ but it is the ubiquity of air pollution and ambient noise, as much as the likely magnitudes of associated risks, which makes them important as potential causes of cardiovascular diseases. Because they share common sources, air pollution and ambient noise are correlated, and this means that any association of cardiovascular disease with either exposure may be masked or confounded by the other. Despite this, most studies have considered traffic noise or air pollution separately, and the study by Kälsch and colleagues² is one of a limited number that have attempted to disentangle their effects on cardiovascular outcomes.³ Although their results are suggestive of independent effects of long-term particulate air pollution and night-time traffic noise on thoracic aortic calcification (TAC), they should be interpreted cautiously.

Air pollution includes a variety of gaseous species, such as carbon monoxide and nitrogen oxides, as well as suspended particulate matter of various sizes. Many of these have been shown in isolation to have adverse effects on cardiovascular health at higher doses, such as those experienced by active smokers of tobacco.⁴ Observational studies also provide substantial evidence of effects on cardiovascular health at lower levels of exposure due to ambient air pollution, particularly for the risk of acute events such as myocardial infarction⁵ or heart failure⁶ in response to short-term increases in pollution over days or hours. Although most people do not experience high levels of ambient noise, it has been hypothesized that even moderate noise could activate stress responses, with detrimental cardiovascular effects, both during daytime activity and during sleep.⁷,⁸

Kälsch and colleagues examined the associations of 1-year average particulate air pollution and traffic noise with the TAC score in 4238 participants in the Heinz–Nixdorf Recall Study, who were also well characterized in terms of both lifestyle and clinical cardiovascular risk factors. They found that higher concentrations of particulate air pollution <10 μm in diameter (PM₁₀) and <2.5 μm in diameter (PM₂.₅), and greater traffic noise at night (between 2200 and 0600 h), were each associated with a higher TAC score. Overall average traffic noise over 24 h and distance to a highly trafficked road were not associated with TAC.

There are a number of reasons to take care when interpreting these findings. First, the statistical evidence is not particularly strong for the associations with traffic noise. The change in TAC score per 5 dB increase in night-time traffic noise was 3.9% [95% confidence interval (CI) 0.0–8.0%] in the model that was adjusted for PM₂.₅ concentration (table 3 in Kälsch et al.). Because the lower bound of the 95% CI is at 0.0% (no change in TAC), the P-value for this estimate is ~ 0.05. Although 24-h traffic noise was not associated with TAC at the P = 0.05 level of statistical significance, the CIs for these estimates are too wide to conclude that night-time noise is more important than noise at other times of day. Secondly, in contrast to the present study of TAC, a previous analysis of coronary artery calcification (CAC) in the same cohort found that greater distance from a major road was associated with increased CAC, while greater concentration of PM₂.₅ was not associated with a change in CAC (traffic noise was not examined directly).⁹ The statistical power of these studies is too low to conclude that the estimates for TAC and CAC (both of which are predictors of coronary artery disease) are inconsistent, but the differences between the headline results suggest that they should be interpreted with caution until they can be replicated.

An important advantage of the study of Kälsch et al. is that in analyses of particulates and traffic noise, each exposure has been adjusted for the other, as well as for other variables which might confound their associations with TAC. Confounding is one of the most important sources of bias in observational studies; an association between an exposure and an outcome is confounded by a third variable when the latter is associated with the exposure and, independently, with the outcome of interest. For example, traffic noise and...
particulates may confound the associations of each other with TAC because they have a common source (road traffic), and because each is hypothesized to have a causal relationship with thoracic aortic calcification (Figure 1). The associations of TAC with traffic noise and particulates are also likely to be confounded by lifestyle risk factors, such as smoking and obesity, because these factors, as well as proximity to road traffic, are associated with socio-economic position. Figure 1, analysed using the DAGitty graphing tool,10 has arrows in green to show the direction of hypothesized causal relationships of particulates and traffic noise with TAC. Sequences of arrows in red (in any direction) show the pathways by which other variables may be confounders; confounding can be controlled for by statistical adjustment for any set of factors which block these pathways. Hence, the total effect of particulates (or of traffic noise) on TAC can be estimated by adjusting for traffic noise (respectively, particulates), in addition to lifestyle factors and socio-economic status.

The results of Kälsch et al.7 appear to suggest that there may be independent associations of night-time traffic noise and particulates on TAC, but their approach can only yield estimates with small biases if all confounders are included and if measurement errors—the differences between the data and the unknown true values—are also small. In the case of modelled particulates and traffic noise, however, uncertainties are present in the model parameters and underlying data, in the approximation of each individual’s location by their residential address, in any smoothing that may occur due to the choice of spatial resolution, and in the choice of time scale. It is therefore possible that random and systematic errors in modelled particulates and traffic noise are actually large, so that measurement error may pose a particularly difficult methodological challenge in studies of this nature.

The effects of measurement error on statistical estimates are not always easy to predict. It is often repeated that in the special case of random measurement errors in a single exposure, estimates of associations are biased towards the null hypothesis of no effect. In general, however, there may be bias either towards or away from the null, and in extreme cases this can even change the apparent direction of an association. These biases are more difficult to predict, and may be larger, when there are multiple sources of error, when the errors in two or more variables are correlated, when one variable is measured with much less error than the other, and when there are important systematic errors (e.g. due to spatial smoothing).11,12 The likely biases due to measurement error can be assessed by regression calibration techniques,13 either based on a separate validation study involving direct assessment of individual exposures, or, where such data are not available, by simulations of the sensitivity of results to plausible forms of measurement error. Without such validation, however, estimates of associations must be interpreted with caution, even when the statistical evidence is otherwise strong.

Although the sensitivity and subgroup analyses in the study of Kälsch et al. are subject to some of the same caveats described above, they include several interesting results which might be replicated in future studies. First, the main analyses of particulates assume a linear relationship between concentration and TAC score, but non-linear analyses suggest an association with PM2.5 and PM10 particulates only below certain thresholds (figure 2 in Kälsch et al.). Previous work has suggested that the relationship of cardiovascular mortality to both ambient air pollution and cigarette smoke is attenuated at higher concentrations,14 and that estimates of the burden of disease due to particulate air pollution are sensitive to the shape of the response of cardiovascular outcomes to the concentration of particulates.15 Secondly, adjustment for intermediate causes of TAC, including blood pressure, only ‘slightly’ reduced the magnitudes of the associations with TAC score (numerical results were not given). As Kälsch et al. discuss, hypertension may be particularly important in the development of aortic lesions, so it is surprising that adjustment for baseline hypertension or systolic blood pressure did not result in more ‘substantial’ reductions. It is again important not
to overinterpret this finding, but it suggests that there could be a greater role for inflammation or other unmeasured intermediate factors, and leaves open the possibility of direct effects on atherosclerosis by respirable particulates which are small enough to enter the blood stream.

The study by Kälsch and colleagues provides new evidence on the associations of pre-clinical atherosclerosis with long-term particulate air pollution and traffic noise, complementing previous studies which have more often focused on short-term exposures and acute cardiovascular events. However, there remain important methodological challenges in estimating the separate effects of long-term air pollution and traffic noise on cardiovascular outcomes. Larger studies are certainly needed to provide estimates which have greater statistical precision, but validation of modelled individual exposures must also become routine, so that the estimates can be shown to be unbiased, as well as precise.

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References


