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Dear Bob,

I am writing in response to your request for comments on the paper by Miller et al reporting on the association of air pollution and cardiovascular events in women based on the rather large Women's Health Initiative (WHI) Observational Study.

I am not entirely certain just what point the committee wanted to explore but it seems from your note that some were surprised by these findings in women. I am not. The average age of women in this study was 63 years and that is more than 10 years beyond the average age for the menopause. In that population coronary heart disease and many of its manifestations are almost as common in women as in men. There are important differences between men and women in relation to coronary heart disease and these are not fully understood. For example in FRISC II and RITA 3 the five year outcome after randomisation to either medical treatment or angiography with intervention, if appropriate, showed benefit in men but not in women. Other studies have shown that various drugs provide benefit in men and not in women. There has in the literature been much speculation that these and other differences may be related to the anatomy and biology of atherosclerosis within the coronary arteries in women. The size of the coronary arteries may also be relevant.

The WHI study has the advantage of including a large number of persons followed over a long period of time. More importantly the cause of death and the documentation of clinical events during life were carefully recorded with pre stated criteria. Nevertheless there are one or two rather surprising points.

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Air pollution seemed to be associated with almost all manifestations of coronary heart disease with the exception of myocardial infarction. It may be that the definition of myocardial infarction used in this study identified large infarcts rather than more minor events associated with chest pain and a rise in troponin. Those would have been classified as other coronary events. A possible explanation might be that air pollution does not impact on the rupture of an atheromatous plaque causing a large myocardial infarction but does affect the accretion of platelets on an eroded or fissured plaque leading to a more minor coronary syndrome. That is not a powerful but rather a speculative argument.

I was surprised that the relationship existed only with PM 2.5 and not with PM 10 or any specific gas. There may be some methodological problem leading to that observation.

I looked at the supplement and was disappointed not to be able to find any data on total mortality or any relation with respiratory symptoms or lung disease. These authors must have that data and the omission is disappointing. It is possible (and probable) that they are preparing another paper on that issue. It is an important point because there should be data here specific to women relating to the question of just how much of the harm caused by air pollution relates to heart or lung disease.

In the paper they discuss mechanisms and of course it is easy to suggest that some of those mechanisms may differ between men and women. That would need much further research, and difficult research, to establish.

Overall I thought this was a rather important paper confirming previous information, identifying that the problem existed in women and extending the effect from mortality to cardiovascular events. There are clear implications for policies to promote public health.

Kind regards.

Yours sincerely

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