

## Peer Review File

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### Reviewer comments

Comment 1: The correlations between DNA methylation and essential hypertension were the crucial topic in the review. Whether there were else effects of environmental pollutants on epigenetic modifications, except DNA methylation?

Reply 1: In addition to DNA methylation, there are additional effects of environmental pollutants on epigenetic modifications, including non-coding RNAs and histone modifications. However, most of the studies on this topic focused on DNA methylation. Evidence about histone modification and non-coding RNAs remains scarce or inconsistent. Moreover, the main mechanism of epigenetic modification related to hypertension by environmental pollutants is DNA methylation. We added some data on page number 4, second paragraph, to address the question.

Comment 2 In the introduction, it was proposed to add related reference (DOI: 10.21037/apm-20-2265) about essential hypertension.

Reply 2: The title of the proposed reference does not relate to our paper. The title is Associated factors of orthostatic hypotension in the elderly essential hypertension patients and the relationship between orthostatic hypotension and early renal damage.

Comment 3 What were the correlations between inflammation and essential hypertension?

Reply 3: Long-term inflammation process increases ROS production, causing oxidative stress, which leads to endothelial dysfunction. Endothelial function is to regulate blood vessel tone and structure. In chronic inflammation, NO bioavailability decreases, disrupting its main function as a vasodilator so that blood vessel relaxation and vasodilatation are impaired.

Mechanisms of the correlation of inflammation and hypertension are stated in some

parts of the text; Page 7, paragraph 1, lines 4 to 7, and page 8, paragraph 1, lines 1 to 6

A paragraph on inflammation and hypertension was added, starting on page 5

Comment 4 How about the effects of water pollutants on essential hypertension? Please state in the text.

Reply 4: A paragraph about water pollutants on essential hypertension was added, starting on page 12

Comment 5 How to alleviate and treat the effects of environmental pollutant on hypertension? Please state in the text.

Reply 5: Some of the proposed therapies to alleviate and treat the effects of environmental pollutants on hypertension include personal-level interventions which include lifestyle modifications and personal protective equipment, such as high-efficiency home air filtration, which has been validated in studies, as well as portable air cleaners. Chelation therapy for lead and cadmium has been shown to significantly reduce major adverse cardiovascular effects such as myocardial infarction, stroke, coronary revascularization, or hospitalizations for angina, in patient with stable ischemic heart disease. However, no studies have shown chelation infusions to decrease hypertension.

Data about therapies to alleviate and treat the effects of environmental pollutant on hypertension are under the title personalized medicine therapies to mitigate the effects of environmental pollutants on hypertension. The title was modified for better understanding.