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# Editorial commentary: Ecology of cardio-metabolic diseases: Low-income countries also matter

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Improvement in exposure assessment methods and technologies over the recent years has now facilitated studying mixtures of environmental exposures and their health effects. The review by Argacha et al. in trends in cardiovascular medicine [1] summarizes the evidence on the effects of non-air related pollutants, and their potential mechanisms on the cardiovascular system.

Air pollution and other environmental exposures that are difficult to modify at the individual level are estimated to be responsible for more than a quarter of global disability-adjusted life years [2]. Cardiovascular diseases rank first in the contribution to the global disease burden [3]. Therefore, future studies on the contribution of the broader exposome to the cardiovascular disease burden are of great relevance. But what is the benefit of studying the exposome as opposed to single exposures?

First, the availability of more precise and parallel estimates for exposures that are correlated in a spatially and temporally heterogeneous fashion improves causal understanding of single risk's independent health effects. From a policy perspective, it is important to regulate these agents in which lowering their levels or concentrations lead to improved health.

Second, as evidenced by the review [1], different exposures such as air pollution, transportation noise, food toxicants, radiation, and green space share biological pathways such as low grade systemic inflammation, oxidative stress, endothelial dysfunction and stress responses [4–8]. These shared pathways are what one would call "public health relevant pathways". Intervening on these pathways holds promise for a considerable decrease in disease burden. An improved understanding of shared biological pathways to health effects of exposure 'cocktails' could be achieved through the application of systems biology approaches derived using high throughput technologies. This is presently gaining ground with air pollutants and persistent organic pollutants with regards to DNA methylation [9,10] and with metabolome [11,12], but less so for other pollutants including noise exposure. Overlapping biomarkers of exposure identified through single-omic or cross-omic pathway analyses, which are also predicting cardiovascular morbidities, will point at the molecular level to shared mechanisms across exposures.

Third, the thresholds and dose-response curves in the focus of the review by Argacha et al. deserve reconsideration in the light of environmental mixtures and shared pathways. If environmental factors impact on the same biological networks, their threshold and dose-response curve may depend on the chemical and physical context in which they exert their actions. This also implies that the relative risks as input for population-attributable risks towards the global disease burden need refinement. Current estimates assume independence of risk factor effects [2].

For improved guidance of policy, a better understanding must be gained on prevalent exposure mixtures, their shared biological pathways and health-relevant thresholds and dose-response relationships for single agents in the context of specific mixtures.

As we strive to provide evidence, understand and disentangle mechanisms of the health effects of these pollutants in a mostly western context, there is a great need for evidence from low-income countries. Indeed, none of the evidence reviewed by Argacha et al. was from low-income countries despite the generally-known high exposure levels in these settings. Populations in these settings experience high exposures to environmental toxicants, with almost non-existent regulations. For instance, in a study from Nigeria, average noise levels reached 89 dB in urban areas with

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significant night-time exposures from religious activities [13]. The low-income countries also have the highest burden of consumption of chemical contaminants in food due to poorly-regulated reliance on pesticides for agricultural purposes [14]. The high levels of these adverse environmental factors may also contribute to the growing rates of cardiovascular and other non-communicable diseases in these settings as well as the very high mortality rates from cardiovascular and metabolic diseases.

Although research into these factors could be considered a luxury given the high poverty levels and the fact that income-generating activities may contribute to the high levels of exposure, evidence from these settings will add to the global understanding of the context-specific cardiovascular effects of these exposures, especially in the background of prevalent infectious diseases and resilience to seemingly adverse living conditions. Therefore, to paint a broader picture, and understand the ecology of the cardiovascular system in its entirety, evidence from the low-income countries also matters!

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