

# Air pollution and trajectory of cardiometabolic multimorbidity

Li-Zi Lin,<sup>a</sup> Jin-Hui Chen,<sup>b,c</sup> and Guang-Hui Dong<sup>a,\*</sup>

<sup>a</sup>Department of Occupational and Environmental Health, Guangdong Provincial Engineering Technology Research Center of Environmental Pollution and Health Risk Assessment, School of Public Health, Sun Yat-sen University, Guangzhou 510080, China

<sup>b</sup>School of Public Policy and Management, Tsinghua University, Beijing 100084, China

<sup>c</sup>High-Tech Research and Development Center, Ministry of Science and Technology, Beijing 100044, China



As a long-recognized health risk factor, air pollution is an increasing concern of global public health problem to governments and the public, causing a wide range of health issues, including respiratory, cardiovascular problems, diabetes, endocrine changes, obesity, mental health, and issues of psycho-social well-being and life expectancy.<sup>1</sup> According to the reported information from World Health Organization (WHO), over 90% of the global population lives in areas with high levels of air pollutants exceeding WHO guideline limits and even below the safe levels considered by those standards, air pollution could still be harmful to health. Exposure to air pollution causes 4.2 million premature deaths each year globally, and this annual toll may increase to 6.3 million deaths within the next 20–30 years unless there is a significant intervention.<sup>1,2</sup> The health damage of air pollution is often a chronic, long-lasting, and persistent process which often perturbs cellular and epigenetic signaling pathways triggering inflammation and oxidative stress.<sup>3</sup> Although the adverse associations between air pollution and human health have been well-documented, with most epidemiological studies aimed to address the association of air pollution with one stage of disease development, only a few studies have simultaneously examined the effects of air pollution on the incidence, process, and prognosis of disease, which is considered to shed important implications regarding evidence-based preventive and interventional strategies.

In a recent issue of *eBioMedicine*, Luo et al explored the association of air pollution with cardiometabolic multimorbidity (CMM) and its trajectory using a prospective cohort in the UK with 410,494 middle- and old-age adults.<sup>4</sup> CMM was defined as the co-presence of at least two cardiometabolic diseases (CMDs), such as diabetes, ischemic heart disease and stroke. Clinical diagnosis of CMDs was based on the International

Classification of Diseases, 10th Revision (ICD 10th) from the registers of hospital inpatient visits. Exposure to fine particles (PM<sub>2.5</sub>) and nitrogen dioxide (NO<sub>2</sub>) was determined using a land-use regression model developed by the European Study of Cohorts for Air Pollution Effects (ESCAPE). The authors reported an increased risk of almost all phases of CMM progression when exposed to higher air pollution. The phases include the development of first cardiometabolic disease (FCMD), the transition from FCMD to CMM, and the death from baseline and FCMD. Further, the impact of PM<sub>2.5</sub> and NO<sub>2</sub> on disease-specific transitions also differed by diabetes, stroke and ischemic heart disease.<sup>4</sup> The main advantages of this work are 1) the cohort design with large sample size and long follow-up periods (from enrollment until death) allows us to establish a causal association of long-term exposure to air pollution with the trajectory of CMM; 2) the use of multi-state models helps address the effects of air pollution on CMM progression and rules out the competing risk from death. Establishing causality and exploring the excess risk of air pollution to CMM are indispensable to include CMM as an outcome exposed to air pollution in assessments of global disease burden and developing relevant health protection strategies. These findings add invaluable knowledge to this research area and provide important implications for countries and areas vulnerable to air pollution problems.

Despite that this much-needed study sheds light on the intricate association of air pollution and the multimorbidity trajectory, several fundamental questions remain unanswered. First, the authors only assessed the impact of PM<sub>2.5</sub> and NO<sub>2</sub> and did not consider the effects of other pollutants like sulfur dioxide, ozone, and carbon monoxide. In a real-time scenario, people are generally exposed to multi-pollutant mixtures; hence, multi-pollutant weighted models should have been used to address the collinearity issue. Second, ultrafine particles (PM<sub>0.1</sub>) may pose greater toxicity to human health because they can enter the brain directly via the olfactory bulb carrying more adsorbable hazardous components.<sup>5</sup> Nonetheless, few studies have investigated the role of PM<sub>0.1</sub>. Third, the harmful health effects of PM are governed both by the size fraction and chemical constituents imparting differential toxic characteristics to PM, resulting in various health effects.<sup>6</sup>

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\*Corresponding author. Department of Environmental and Occupational Health, Guangdong Provincial Engineering Technology Research Center of Environmental Pollution and Health Risk Assessment, School of Public Health, Sun Yat-Sen University, No. 74 Zhongshan Road 2, Yuexiu District, Guangzhou, Guangdong Province 510080, China.

E-mail addresses: [donggh5@mail.sysu.edu.cn](mailto:donggh5@mail.sysu.edu.cn), [donggh512@hotmail.com](mailto:donggh512@hotmail.com) (G.-H. Dong).

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Taking into consideration the global phenomenon of population aging with declining fertility and increased longevity, CMM has become a rising public health challenge due to its damage to human health. This work by Luo et al provides crucial epidemiological evidence linking air pollution and CMM progression trajectory. It's of importance to develop primary and secondary prevention strategies regarding CMM by considering improving air quality, which might further reduce the societal burden. When understanding disease burden related to air pollution and developing health promotion strategies, CMM is the need of the hour in this aging era.

#### Contributors

Literature search: L.-Z.L., J.-H.C., and G.-H.D.; Data collection: L.-Z.L. and G.-H.D.; Data interpretation: L.-Z.L. and G.-H.D.; Writing: L.-Z.L., J.-H.C., and G.-H.D. All authors read and approved the final version of the manuscript.

#### Declaration of interests

All authors have nothing to declare.

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