Opinion Paper

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Contribution of laboratory medicine and emerging technologies to cardiovascular risk reduction via exposome analysis: an opinion of the IFCC Division on Emerging Technologies

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Abstract: This opinion article highlights the critical role of laboratory medicine and emerging technologies in cardiovascular risk reduction through exposome analysis. The exposome encompasses all external and internal exposures an individual faces throughout their life, influencing the onset and progression of cardiovascular diseases (CVD). Integrating exposome data with genetic information allows for a comprehensive understanding of the multifactorial causes of CVD, facilitating targeted preventive interventions. Laboratory medicine, enhanced by advanced technologies such as metabolomics and artificial intelligence (AI), plays a pivotal role in identifying and mitigating these exposures. Metabolomics provides detailed insights into metabolic changes triggered by environmental factors, while AI efficiently processes complex datasets to uncover patterns and associations. This integration fosters a proactive approach in public health and personalized medicine, enabling earlier detection and intervention. The article calls for global implementation of exposome technologies to improve population health, emphasizing the need for robust technological platforms and policy-driven initiatives to seamlessly integrate environmental data with clinical diagnostics. By harnessing these innovative technologies, laboratory medicine can significantly contribute to reducing the global burden of cardiovascular diseases through precise and personalized risk mitigation strategies.

Keywords: exposome; cardiovascular disease; epigenetics; metabolomics; artificial intelligence; environment

Most human diseases are fueled by both genetic and environmental factors. The current generation of 21st century adults live in an environment undergoing substantial economic, social, and technological transformations. Sustainability is a critical challenge in healthcare and laboratory medicine which requires a multi-dimensional

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approach aimed at improving population health [1]. Cardiovascular diseases (CVD) remain a major global health challenge, influenced by a combination of genetic, lifestyle, and environmental factors. It is important to mention that environmental refers to a combination of unhealthy lifestyle, pollution, and psychosocial stress as well as increasing awareness of the impact of the natural, built, and social environments on common pathways that heighten susceptibility to chronic non-communicable diseases. The concept of exposome, which refers to the comprehensive measure of all the exposures an individual encounters from conception onward, is essential for understanding these multifactorial interactions. Research has demonstrated that various environmental exposures, such as air pollution, dietary patterns, physical activity, and socio-economic status, significantly impact cardiovascular health [2–4]. Despite these findings, there is still a gap in effectively integrating these diverse environmental exposures with laboratory data to improve CVD outcomes. This paper aims to address this gap by exploring how the integration of the exposome with emerging technologies in modern laboratory medicine, such as metabolomics and artificial intelligence (AI), can enhance the prediction, prevention, and treatment of CVD. By leveraging these emerging technologies, we can gain deeper insights into the biological mechanisms through which environmental exposures influence cardiovascular health, identify novel biomarkers for early detection, and develop personalized intervention strategies to mitigate CVD risk.

The exposome is a comprehensive measure of all the exposures an individual encounters throughout their life and the impact of these exposures on health. It encompasses the entirety of external (exogenous) and internal (endogenous) exposures from conception onwards, distinguishing, characterizing, and quantifying the etiologic, mediating, moderating, and co-occurring risk and protective factors, and their relationship to disease. The exposome specifically examines the biological mechanisms and pathways through which chemical and non-chemical environmental exposures are linked to the onset, progression, and outcomes of CVD. In particular, the exposome outlines the harmful biochemical and metabolic changes that occur in the human body due to the combination of different environmental exposures throughout life. In this context, it is essential to assess the exposure-related changes in metabolic and biochemical pathways and link them to CVD outcomes. Moreover, assessing both genetic and environmental risk factors prevalent among family members can aid in cascade screening, thereby identifying asymptomatic individuals who are at risk of developing CVD in the future. Implementing an approach that utilize potential biomarkers, which integrate the genotypic substrate and including "omics" technologies, is crucial for stratifying the risk of developing CVD events [2].

Laboratory medicine plays a critical role in this field by utilizing innovative technologies and precision diagnostics to measure and mitigate these exposures, thereby reducing cardiovascular risks [5]. The exposome includes all non-genetic exposures from conception onwards that contribute to health outcomes [2, 6]. While traditional laboratory medicine has concentrated on biochemical markers and genetic predispositions, the integration of exposome data significantly shift towards a more comprehensive approach in healthcare. Modern analytical techniques now facilitate the identification of biomarkers linked to environmental exposures, providing a deeper understanding of the interactions between external factors and cardiovascular health [6, 7]. OMICS (epigenomics, genomics, proteomics, transcriptomics, and metabolomics) approaches are essential in tackling the challenges against CVDs because they offer comprehensive insights into how environmental exposures affect biological systems. Although genome-wide association studies (GWAS) primarily focus on genetic factors, integrating GWAS data with exposome research can provide a more comprehensive view of how genetic predispositions interact with environmental exposures to influence disease outcomes. This combined approach can offer new insights into early detection and possible therapeutics of CVDs [8].

Emerging technologies such as metabolomics and artificial intelligence (AI) are revolutionizing the field of healthcare and laboratory medicine by enhancing our ability to analyze the exposome and its impact on cardiovascular health [6, 7, 9]. These technologies offer innovative insights and methodologies that tackle the complexities of environmental influences on health. Metabolomics provides a sophisticated analytical approach capable of identifying rapid metabolic changes triggered by environmental factors [7, 9]. For instance, recent studies have demonstrated the utility of metabolomics in detecting specific metabolic alterations associated with exposure to pollutants, which are linked to an increased risk of CVD. An essential component of exposome analysis relies also on non-targeted analysis, which extends beyond traditional targeted methods. Non-targeted analysis is crucial for discovering new or unknown pollutants and their metabolites in biological and environmental samples. This approach is not limited to untargeted metabolomics but also encompasses the identification of previously unrecognized chemical entities, providing a broader understanding of the environmental contributors to CVD [10].

Metabolomics analyzes a broad spectrum of small molecules such as lipids and amino acids, which act as biomarkers for various physiological and pathological states. Metabolomics allows for an in-depth characterization of metabolic responses to environmental exposures which traditional biochemistry might overlook. By integrating metabolomics into exposome research, scientists can detect subtle biochemical shifts that precede observable symptoms, thereby enabling earlier intervention in disease processes.

AI tools, including advanced deep learning techniques such as AlphaFold 3, are increasingly being utilized to predict disease risk based on a patient's unique exposome and genome. These technologies extend beyond traditional machine learning by offering molecular-level insights into disease processes, which is particularly valuable in understanding the complex mechanisms underlying cardiovascular diseases [11]. Furthermore, the application of explainable AI allows researchers to uncover detailed associations between environmental exposures and CVD at a molecular level, providing a more transparent and interpretable approach to AI-driven diagnostics [2]. AI, on the other hand, brings powerful computational capabilities to exposome research, handling vast and complex datasets with unprecedented efficiency [6, 12]. AI leverages machine learning algorithms to uncover patterns and associations within the data that might not be evident through conventional analysis. For instance, AI can analyze geographical information systems and environmental sensor data to predict disease risk or identify potential environmental hazards without direct physical testing. Furthermore, AI can integrate various data layers – from genomic data to large-scale environmental datasets – creating comprehensive models that simulate the potential impacts of different exposures on human health. AI can also facilitate the analysis of metabolomics data by efficiently processing large datasets, identifying patterns, and uncovering complex relationships that might not be evident through traditional methods. Together, these technologies enable a more nuanced understanding of how environmental factors contribute to cardiovascular risks. By combining AI-driven analytics and metabolomics, researchers can now approach the exposome with a level of precision and depth that was previously unattainable. This integrated perspective not only enhances our understanding of disease mechanisms but also informs more effective prevention strategies that are tailored to the unique environmental and metabolic contexts of individual patients. A recent study has highlighted the value of AI in utilizing exposome data for cardiometabolic risk assessment by developing a machine learning model that effectively predicts the risk of CVD and type 2 diabetes based solely on exposome factors [13]. The model demonstrated performance comparable to more comprehensive integrative models and outperformed the traditional Framingham risk score for CVD prediction, while also showing no bias across key demographics [13]. This underscores the potential of exposome-based AI models as fair and effective tools for early disease risk assessment and prevention.

The integration of these emerging technologies fosters a proactive approach in public health and personal medicine. As we continue to expand our technological capabilities, the potential for significant breakthroughs in predicting, preventing, and treating cardiovascular diseases through exposome analysis looks increasingly promising. The future directions of laboratory medicine will likely focus on harnessing these technologies to develop interventions that are both personalized and preemptive, ultimately reducing the global burden of cardiovascular diseases. Emerging studies, particularly those applying AI to analyze conditions within urban environments, have linked specific environmental characteristics with elevated cardiovascular risks [12]. Additionally, metabolomic research has identified specific metabolic alterations associated with exposure to various pollutants and dietary factors, further reinforcing the connections between environmental exposures and cardiovascular disease pathology [2, 7].

Integrating exposome analytics into clinical practice presents several challenges, including the need for data standardization, complex technological platforms and addressing privacy concerns. Future advancements should aim at developing robust technologies that can integrate environmental data with clinical diagnostics seamlessly. Policy-driven initiatives will be crucial in promoting the adoption of these advanced technologies in healthcare settings across the world [6].

In conclusion, integrating laboratory medicine with cutting-edge technologies like AI and metabolomics to analyze the exposome holds significant potential in advancing the prevention of CVD. While these approaches promise to enhance individual patient care and strengthen public health strategies, further research and technological advancements are necessary to fully realize their impact.

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