

## **Causal inference between bioavailability of heavy metals and environmental factors in a large-scale region**

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The causation between bioavailability of heavy metals and environmental factors are generally obtained from field experiments at local scales at present, and lack sufficient evidence from large scales. However, inferring causation between bioavailability of heavy metals and environmental factors across large-scale regions is challenging. Because the conventional correlation-based approaches used for causation assessments across large-scale regions, at the expense of actual causation, can result in spurious insights. In this study, a general approach framework, Intervention calculus when the directed acyclic graph (DAG) is absent (IDA) combined with the backdoor criterion (BC), was introduced to identify causation between the bioavailability of heavy metals and the potential environmental factors across large-scale regions. We take the Pearl River Delta (PRD) in China as a case study. The causal structures and effects were identified based on the concentrations of heavy metals (Zn, As, Cu, Hg, Pb, Cr, Ni and Cd) in soil (0-20 cm depth) and vegetable (lettuce) and 40 environmental factors (soil properties, extractable heavy metals and weathering indices) in 94 samples across the PRD. Results show that the bioavailability of heavy metals (Cd, Zn, Cr, Ni and As) was causally influenced by soil properties and soil weathering factors, whereas no causal factor impacted the bioavailability of Cu, Hg and Pb. No latent factor was found between the bioavailability of heavy metals and environmental factors. The causation between the bioavailability of heavy metals and environmental factors at field experiments is consistent with that on a large scale. The IDA combined with the BC provides a powerful tool to identify causation between the bioavailability of heavy metals and environmental factors across large-scale regions. Causal inference in a large system with the dynamic changes has great implications for system-based risk management.