Mendelian randomization: Can we see the forest for the IVs?

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When randomized trials are not feasible, the only hope to empirically inform clinical and policy medical decisions is to estimate causal effects using observational studies. However, unmeasured confounding makes using classical epidemiologic approaches to estimate causal effects challenging. One promising alternative is Mendelian randomization, a form of instrumental variable (IV) methods that proposes leveraging genes as natural experiments. The past decade has seen an increased adoption of Mendelian randomization strategies in epidemiology, often touting Mendelian randomization as the future of epidemiology and “the” causal method. Concurrently, the past decade has also seen major developments in Mendelian randomization methodology, including improved methods for using genome-wide association study data to leverage many genetic variants as proposed but perhaps imperfect IVs. The focus of this talk will be on connecting current and on-going advancements in IV methods to broader discussions of how to combine data with biologically plausible and transparent assumptions to test for and estimate causal effects. An emphasis will be placed on how Mendelian randomization studies are conducted and interpreted in public health research.

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