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Multi-polygenic risk score approach to trait genetic burden for the development of CKD and CVD

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Objectives : Chronic kidney disease (CKD) and cardiovascular disease (CVD) share common genetic and environmental risk factors, contributing to their high comorbidity. While polygenic risk scores (PRS) have been widely used for predicting disease susceptibility, their predictive power for complex traits remains limited. This study aimed to develop a multi-PRS approach integrating genetic risk for multiple traits and assess its predictive utility for CKD and CVD.

Methods : We utilized genetic and phenotypic data from the UK Biobank (N=403,642) to construct PRSs for CKD, CVD, and related metabolic traits. PRSs were derived using multiple methods, including LDpred and PRS-CS, and optimized for classification performance. The final models incorporated significant PRSs through stepwise selection, followed by adjustment for modifiable lifestyle factors such as smoking, alcohol consumption, and dietary intake. Statistical analyses included logistic regression and De Long's test to compare predictive accuracy.

Results : The multi-PRS models significantly improved CKD and CVD prediction over single-disease PRS models, increasing classification accuracy by 1.5% and 0.4%, respectively. PRSs for hypertension and type 2 diabetes were major contributors to CKD and CVD risk, while dyslipidemia PRS further enhanced CVD prediction (Fig 1, 2). Incorporating laboratory PRSs, including serum creatinine, BMI, HDL-C, and triglycerides, refined risk estimation, with a 0.9% and 0.3% increase in CKD and CVD prediction accuracy, respectively. Modifiable lifestyle factors had varying influences on genetic risk associations, highlighting their complex interplay in disease development.

Conclusions : A multi-PRS framework integrating genetic susceptibility to multiple traits enhances CKD and CVD risk prediction. This approach provides a more comprehensive genetic risk assessment and underscores the importance of considering metabolic and environmental interactions in disease prevention and management.

Fig 1.png

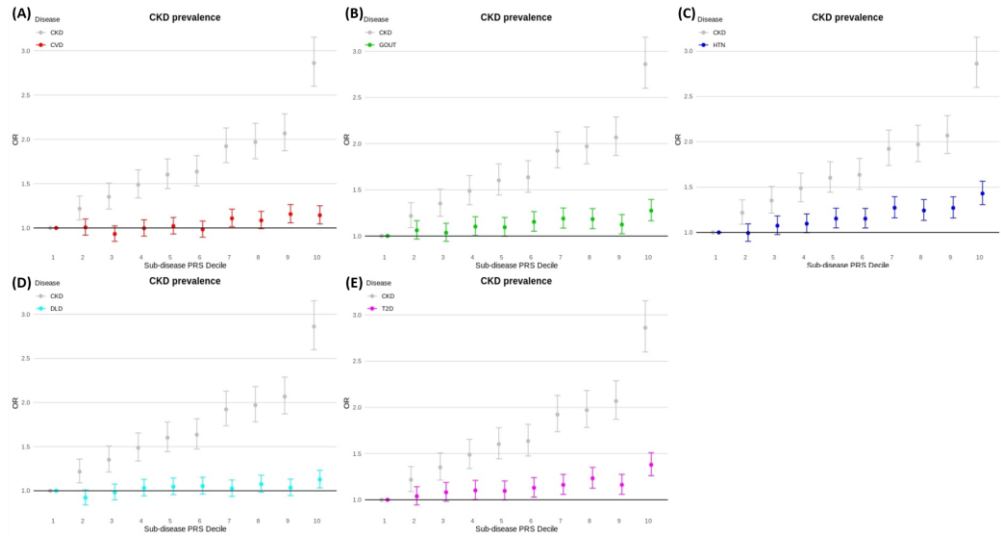


Fig 1.png

