# Phenome-Wide Association Study of Echocardiographic Measures of Cardiac Structure and Function in the Penn Medicine BioBank

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**Introduction:**

We performed a phenome-wide association study (PheWAS) to investigate associations between quantitative measures of cardiac structure and function and clinical phenotypes at scale.

**Methods:**

Transthoracic echocardiography (TTE) measurements including ejection fraction (EF), left ventricular internal diameter in diastole (LVIDd), interventricular septal thickness (IVSd), and left ventricular posterior wall thickness (LVPWT) were extracted either from the electronic health record or directly from TTE images using the PanEcho deep learning model. PheWAS were performed among up to 19,079 Penn Medicine BioBank participants with available echo, genotypic, and clinical data, after adjusting for age, sex, and 10 genetic principal components. Significance was assessed after Bonferroni correction.

**Results :**

The average age was 55.2 years, 50% were female, and 69.3% had European (EUR) genetic ancestry. Overall, we observed 955 significant echo-trait associations across the 4 TTE measures, including: EF and heart failure with reduced ejection fraction (OR = 0.92, p <1E-300), ventricular tachycardia (OR = 0.94, p <1E-300), and mitral valve disorders (OR = 0.98, p = 8.37E-58); LVIDd and cardiomyopathy (OR = 2.805, p = 5.06E-296), hypertensive heart disease (OR = 1.73, p = 3.59E-59), and arrhythmias (OR = 1.49, p = 3.25E-63); IVSd and hypertrophic cardiomyopathy (OR = 414.6, p = 3.05E-125), hypertension (OR = 8.520, p =3.13E-109), and aortic valve disorders (OR = 7.597, p = 1.64E-102); and LVPWT and heart failure with preserved ejection fraction (OR = 13.3, p = 3.38E-96), heart valve replaced (OR = 8.35, p = 8.27E-54), and endocarditis (OR = 4.72, p = 3.82E-13). Results were similar using PanEcho-derived measurements.

**Conclusions:**

Expected and novel associations between echo measurements and clinical phenotypes were observed. Limitations include selection bias in who received echo and reverse causality; directionality of associations should be interpreted cautiously. Future work will leverage genotype data to investigate potentially causal associations using Mendelian randomization.