SIGNIFICANCE STATEMENT

Many patients with autosomal dominant polycystic kidney disease (ADPKD) and autosomal dominant polycystic liver disease (ADPLD) remain asymptomatic as the disease progresses, and estimating prevalence of these conditions is challenging because of incomplete clinical ascertainment. The authors' analysis of population-based sequencing data of genes involved in ADPKD and ADPLD found that protein-truncating and clinically confirmed mutations provide a lifetime risk of ADPKD of at least nine cases per 10,000. Protein-truncating mutations in genes causative of ADPLD are as common as 20 cases per 10,000. Individually rare variants in genes of potential relevance as ADPKD modifiers are cumulatively common, but most have uncertain clinical significance. Further research using exome or targeted gene resequencing in patients with ADPKD will help evaluate these rare variants.