The diagnostic accuracy of ultrasound and genetic tests for the diagnosis of autosomal dominant polycystic kidney disease: A systematic mapping review

MT41

S Harnan[1], M Gittus[1], L Falzon[1], M Durkie[2], O Mandrik[1], A Ong[1], J Fotheringham[1]

1. University of Sheffield
2. Sheffield Diagnostic Genetics Service, Sheffield Children's NHS Foundation Trust

Despite technological advances, sensitivity of genetic tests for polycystic kidney disease was static over time

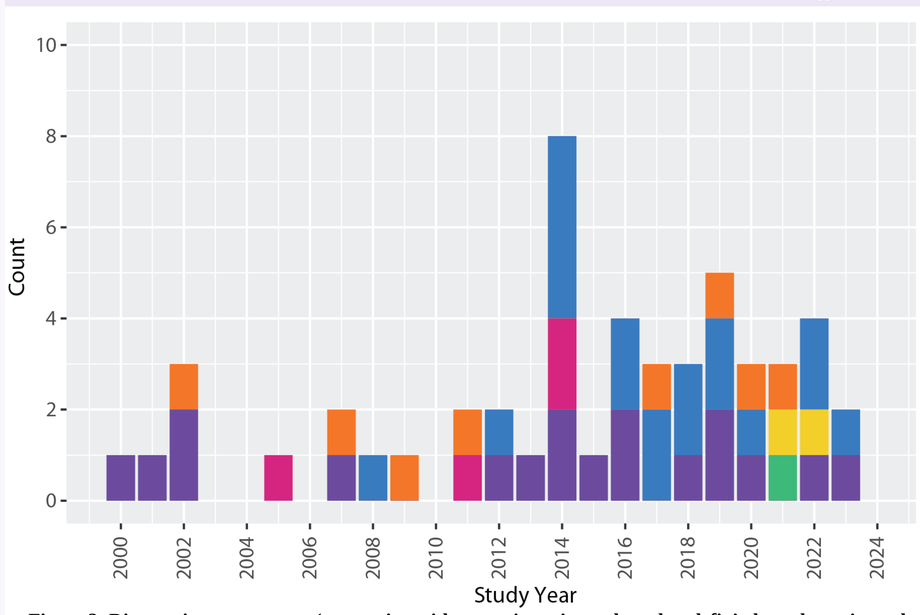

Figure 2: Diagnostic test accuracy (proportion with genomic variants classed as definitely pathogenic, pathogenic, likely pathogenic and probability pathogenic or similar terms), stratified by genes targeted and recruitment criteria, by study publication year.

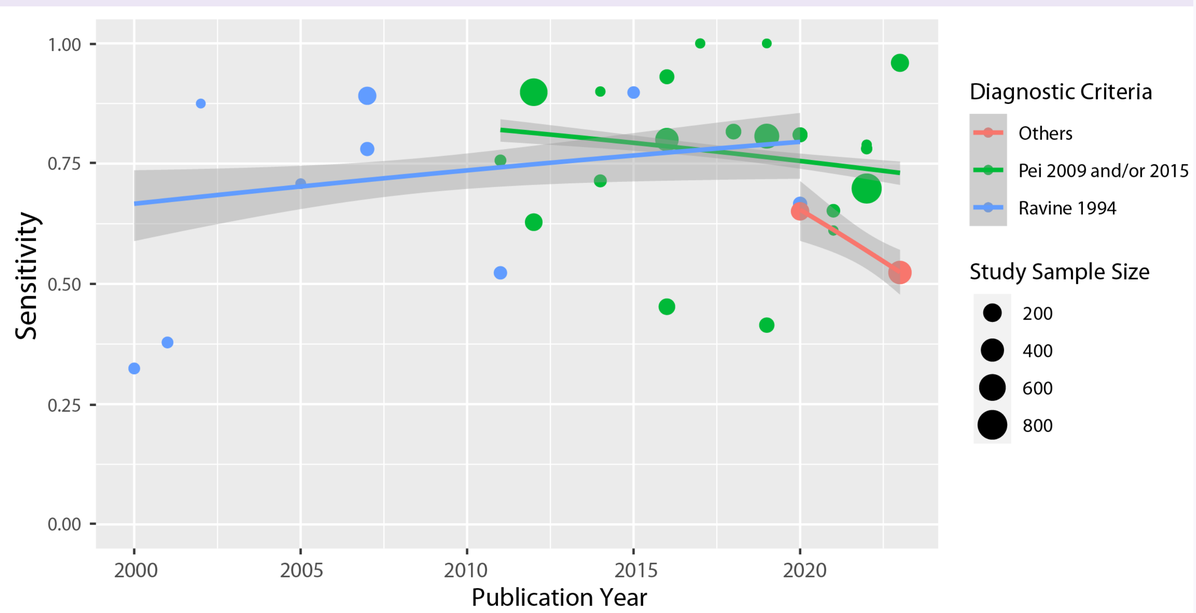

Figure 3: Genomic test technology by year of study publication

Background

Autosomal Dominant Polycystic Kidney Disease (ADPKD, estimated prevalence: 1 in 1000) causes kidney failure and is inherited by 50% of offspring.

Diagnostic uncertainty due to poor ultrasound sensitivity under age 40 argues for increasingly affordable genetic testing, which may provide earlier diagnosis.

Continued identification of new pathogenic variants and evolving genetic technologies (figure 1) justify systematic mapping of genetic and ultrasound diagnostic test accuracy (DTA).

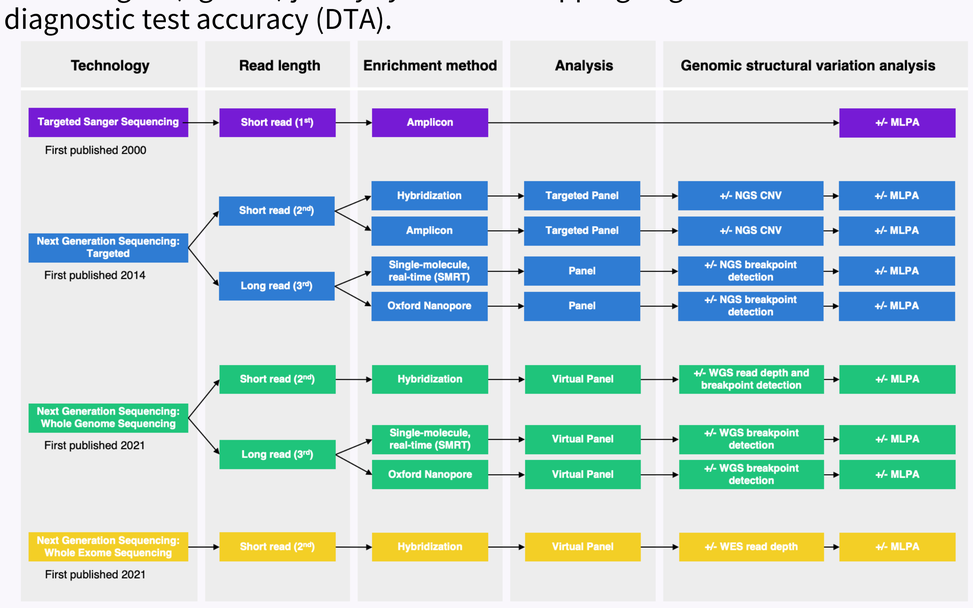

Figure 1: Taxonomy of genomic technologies included in the review

Methods

Mapping reviews by design are descriptive in nature, do not include statistical synthesis, and use graphical, tabular and narrative methodologies to characterise the literature.

Medline, Embase and Cochrane were searched (August 2023) for studies of genetic or ultrasound tests in those clinically diagnosed or at 50% risk of inheriting ADPKD. A validated search filter to identify diagnostic studies was applied. Relevant conferences from the last 3 years were also searched.

Two reviewers separately used Covidence with AI-assisted study prioritisation to screen studies according to the inclusion criteria, considering first the title and abstract, then examining the full texts of the remaining articles.

Acceptable reference standards were definitive imaging or genetic confirmation. Studies reporting sensitivity and specificity, or detection rates if insufficient DTA evidence, were included and mapped.

The evidence map was primarily analysed according to test type (figure 1) and population (referenced ultrasound defintions[1,2,3]).

Results

From 1029 non-duplicate titles retrieved, 51 genetic and 7 ultrasound studies were included. There were no studies of genetic tests in people at 50% risk.

Genetic Studies

Amongst studies in patients with clinical diagnoses, genetic test methodologies were highly heterogeneous (figure 2).

The recruitment criteria varied: Ravine *et al.,*1994[1]criteria, which targeted *PKD1* patients, were used in 16 studies, Pei *et al.,*2009[2] and its extension Pei *et al.,*2015[3] (n=25 studies) should in theory recruit people with both *PKD1* and *PKD2* variants. Other imaging criteria (Torres *et al.,*2012, Torres *et al.,*2017, KDIGO guideline criteria) were used in a further 5 studies.

The genes targeted by genomic tests also broadened over time.

Genomic detection rates (range 60% to 100%) did not appear to improve over time (figure 3).

Ultrasound Studies

Sensitivity and specificity generally improved with age (figure 4):

The lowest reported were 31% and 88% respectively in *PKD2* patients aged 5-14.

The highest 100% and 100% respectively in multiple gene/age categories) and were worse in *PKD2* patients compared to *PKD1*.

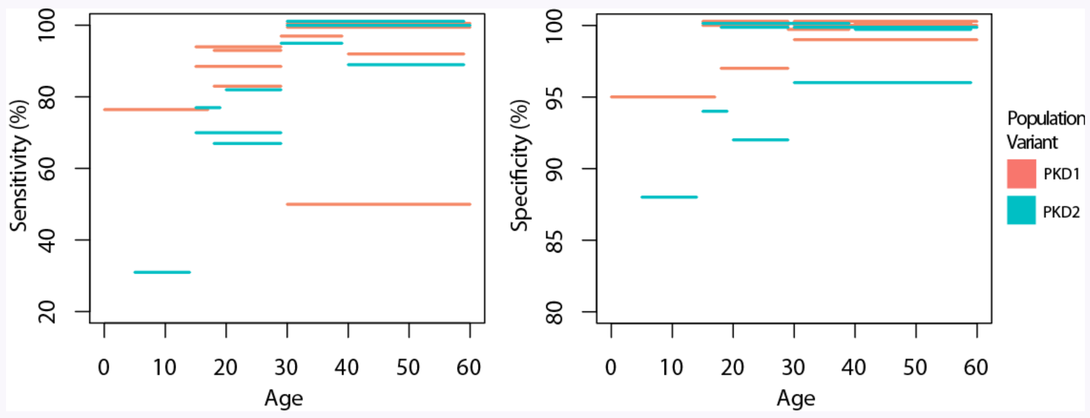

Figure 4 Sensitivity and specificity of ultrasound studies. Each bar represents the sensitivity or specificity for the age range spanned by the bar, as reported by individual studies included in this review.

Conclusions

- **Despite technological advances, genetic test sensitivity was static over time, possibly because clinical diagnostic criteria (and hence populations recruited) widened from *PKD1* to include *PKD2* and other phenotypes.**
- **Relatives of patients whose pathogenic variant is not identified by genetic tests will need serial ultrasound scans with potentially decades of uncertainty.**
- **Unified genomic test taxonomies would facilitate future reviews.**

University of Sheffield

Please contact
s.harnan@sheffield.ac.uk
for additional information

1. Ravine D, Gibson RN, Walker RG, Sheffield LJ, Kincaid-Smith P, Danks DM. Evaluation of ultrasonographic diagnostic criteria for autosomal dominant polycystic kidney disease 1. *Lancet*. 1994;343(8901):824-7
2. Pei Y, Obaji J, Dupuis A, et al. Unified criteria for ultrasonographic diagnosis of ADPKD. *J Am Soc Nephrol*. 2009;20(1):205-12. doi:https://dx.doi.org/10.1681/ASN.2008050507
3. Pei Y, Hwang YH, Conklin J, et al. Imaging-based diagnosis of autosomal dominant polycystic kidney disease. J Am Soc Nephrol. 2015;26(3):746-53. doi:https://dx.doi.org/10.1681/ASN.2014030297