

Diagnostic yield of WGS for detecting pathogenic SNVs in congenital heart disease: a systematic review and meta-analysis

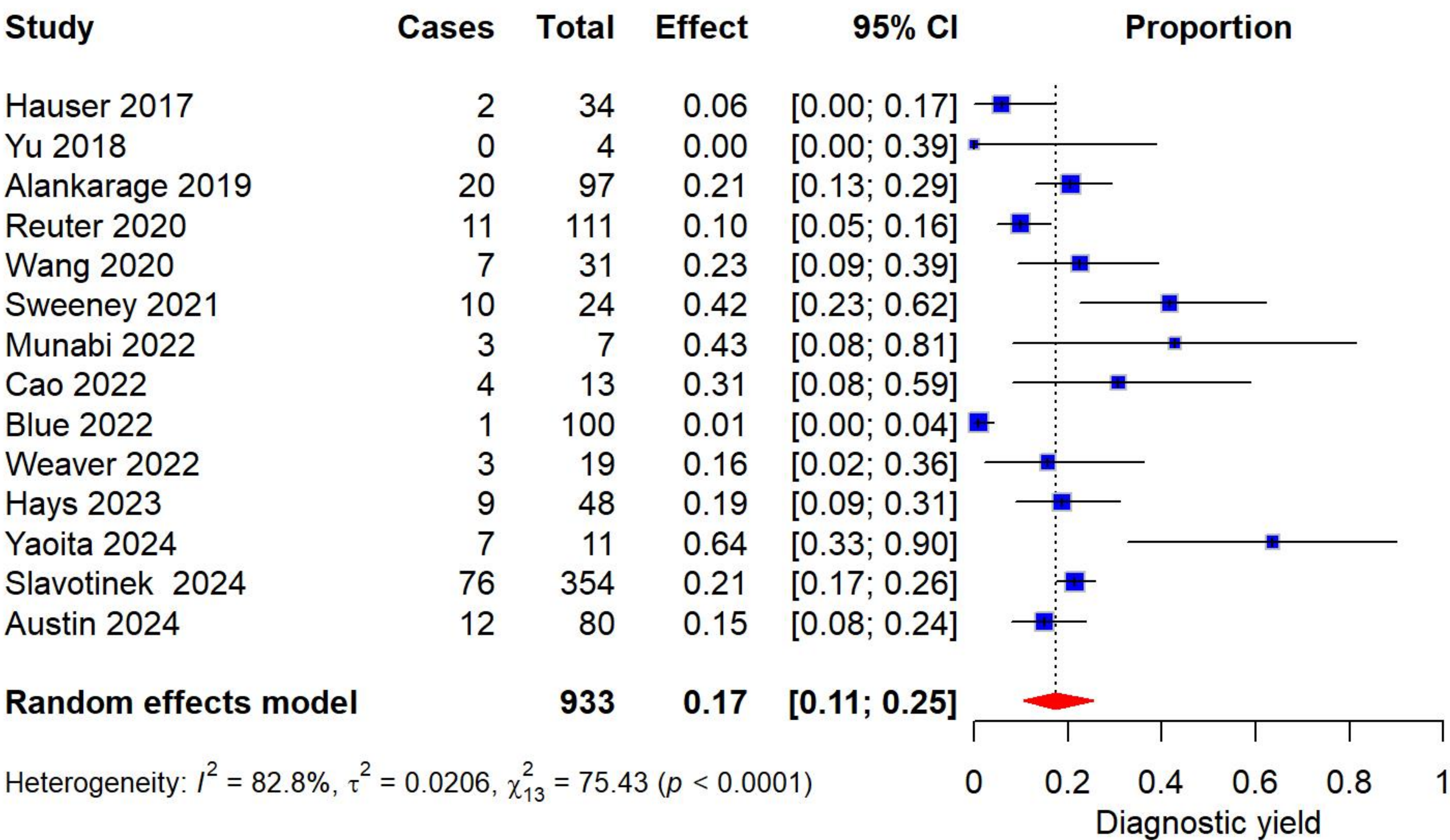
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Objectives

To evaluate the diagnostic yield of whole-genome sequencing (WGS) in identifying pathogenic or likely pathogenic (P/LP) single nucleotide variants (SNVs) in patients with congenital heart disease (CHD).

Methods

A systematic search of the literature was conducted to identify studies involving at least three probands with CHD who underwent WGS. The primary outcome was the diagnostic yield of P/LPSNVs in all CHD cases, as well as isolated and syndromic CHD subgroups.



Results

- Thirteen studies, comprising a total of 933 CDH cases, were included in this systematic review and meta-analysis, among which 165 cases had P/LP SNVs.
- The diagnostic yield of WGS for identifying P/LP SNVs was 17.83% in all CHD cases, 9.83% in isolated CHD, and 22.36% in syndromic CHD.
- Additionally, the yield was calculated based on structural anomalies, resulting in yields of 1.27% for CHD-only cases and 21.66% for CHD with extracardiac anomalies.

Diagnostic yield of WGS in prenatal CHD, stratified by clinical presentation

Classification	WGS Positive (n)	Total WGS (n)	Pooled Proportion % (95% CI)
All cases	165	933	17.83% (10.20%-26.78%)
Prenatally detected CHD only	40	421	10.27% (1.09%-24.54%)
Prenatally detected CHD with extracardiac anomalies	115	441	21.66% (12.60%-32.08%)
Isolated CHD	38	418	9.83% (0.51%-25.20%)
Syndromic CHD	117	444	22.36% (13.26%-32.27%)

Conclusion

WGS surpasses traditional diagnostic methods by providing comprehensive insights into the genetic basis of CDH and guiding multidisciplinary management strategies. Therefore, WGS should be recommended as a routine diagnostic adjunct for patients with CHD.