

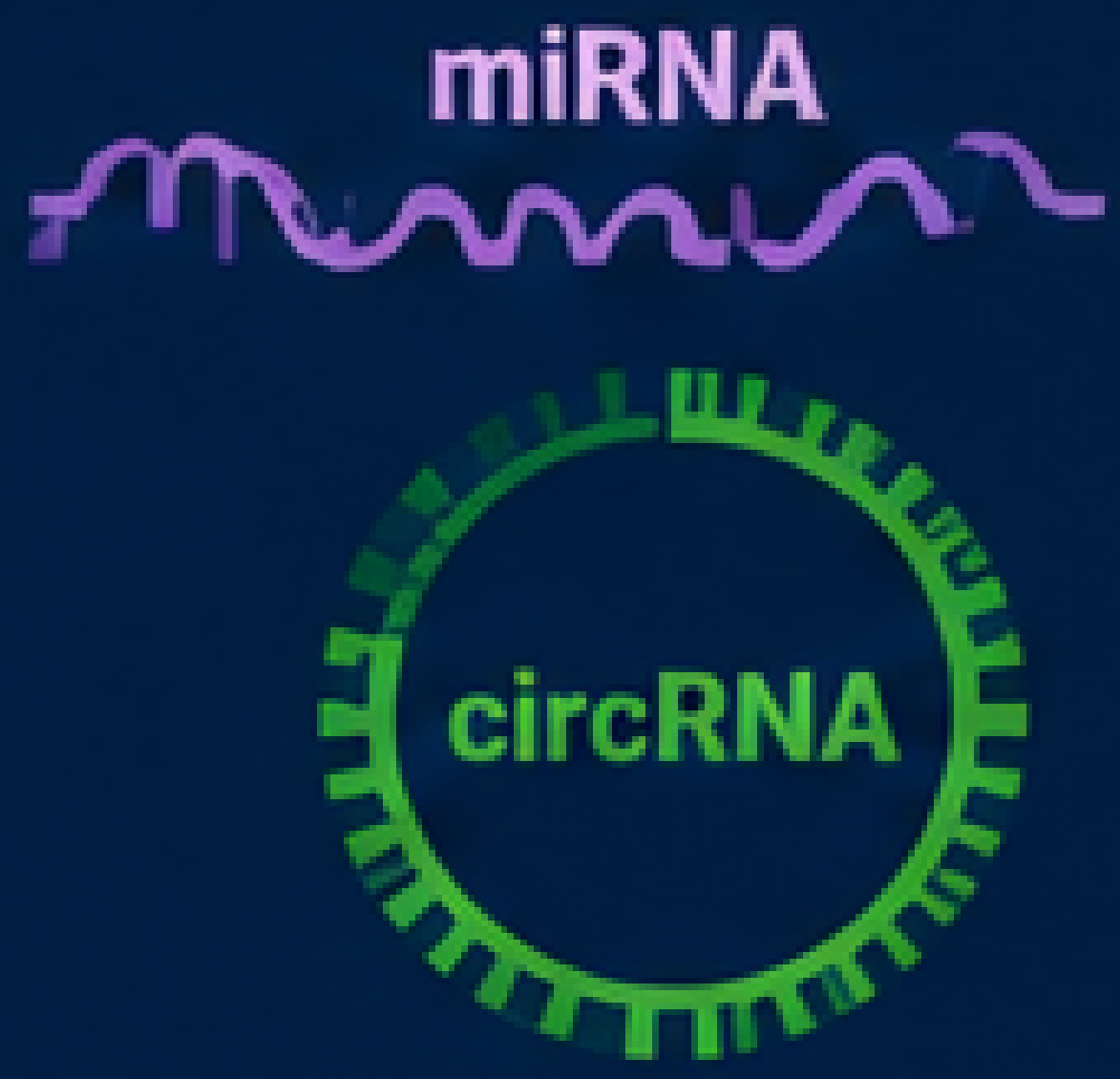
Diagnostic Accuracy of Non-Coding RNAs in Chronic Lymphocytic Leukemia: A Systematic Review and Meta-Analysis

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BACKGROUND

Non-coding RNAs (ncRNAs), including microRNAs (miRNAs) and circular RNAs (circRNAs), have emerged as promising non-invasive biomarkers in chronic lymphocytic leukemia (CLL). Their stability, tissue specificity, and ease of quantification highlight their potential diagnostic utility. This systematic review and meta-analysis evaluated the diagnostic performance of ncRNAs in patients with CLL.



METHODS

A systematic review was conducted according to PRISMA guidelines. PubMed, Embase, Web of Science, Scopus, and ProQuest were searched through January 2024. Case-control and cross-sectional studies evaluating the diagnostic value of ncRNAs in CLL were included. Diagnostic parameters including sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), diagnostic odds ratio (DOR), and area under the curve (AUC) were pooled using random-effects models. Risk of bias was assessed using QUADAS-2, while certainty of evidence was evaluated with the GRADE approach.

PubMed

Embase[®]

Web of Science[™]

Scopus

ProQuest[®]



RESULTS

Fourteen studies involving 934 patients with CLL and 422 healthy controls were included. Nine studies evaluated 19 distinct miRNAs, while five studies assessed eight circRNAs.

	miRNAs (9 Studies)	circRNAs (5 Studies)
Parameter	Pooled Estimate (95% CI)	Pooled Estimate (95% CI)
Sensitivity	0.84 (95% CI: 0.78–0.89)	0.69 (95% CI: 0.63–0.74)
Specificity	0.98 (95% CI: 0.93–0.99)	0.77 (95% CI: 0.71–0.82)
Positive Likelihood Ratio (PLR)	42.19 (95% CI: 11.83–150.48)	3.01 (95% CI: 2.34–3.88)
Negative Likelihood Ratio (NLR)	0.16 (95% CI: 0.11–0.23)	0.40 (95% CI: 0.33–0.49)
Diagnostic Odds Ratio (DOR)	260.25 (95% CI: 61.15–1107.59)	7.51 (95% CI: 4.93–11.44)
Area Under the Curve (AUC)	0.96 (95% CI: 0.93–0.97)	0.80 (95% CI: 0.76–0.83)

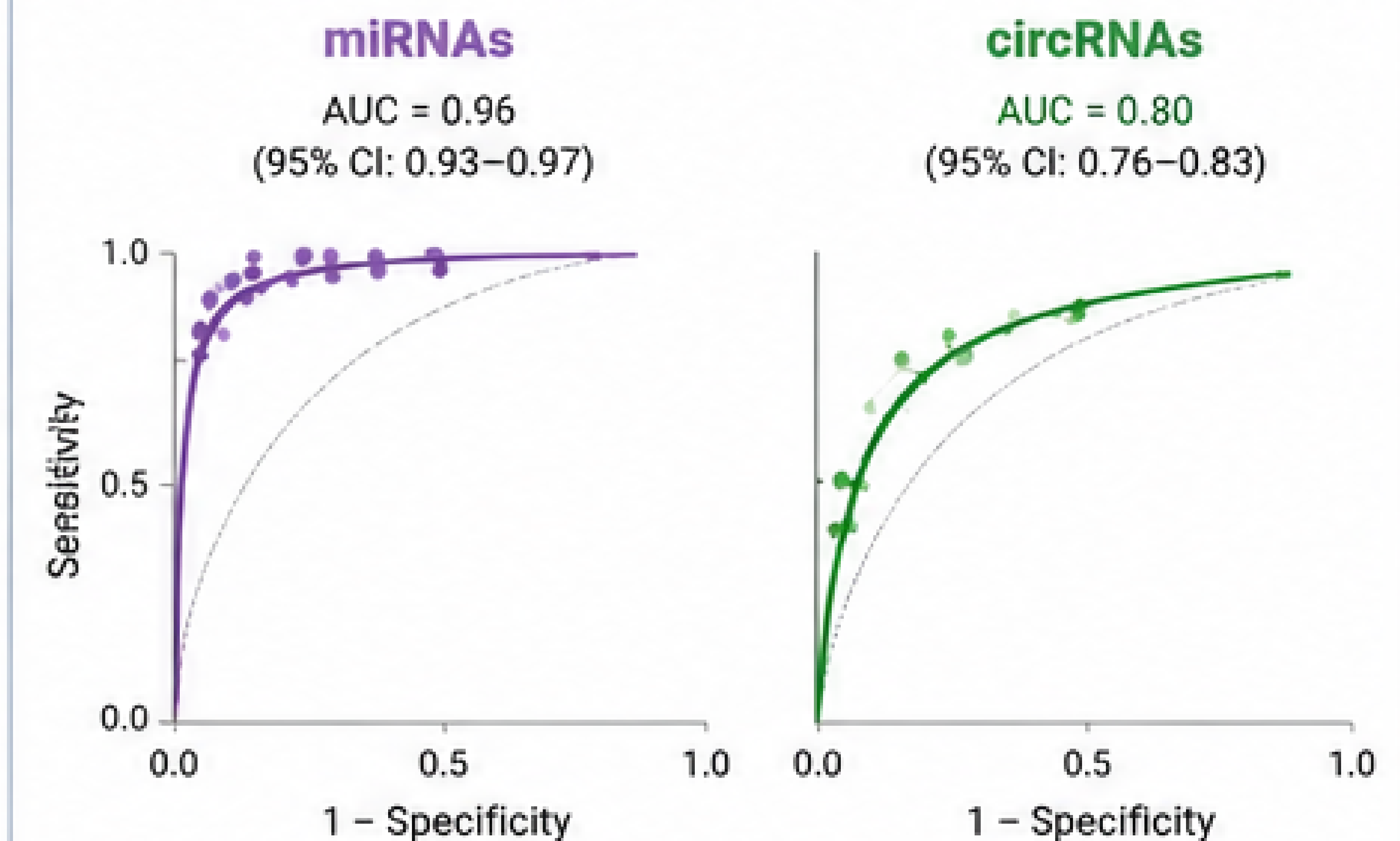


Subgroup analyses showed that studies with high risk of bias and smaller sample sizes consistently overestimated diagnostic performance.

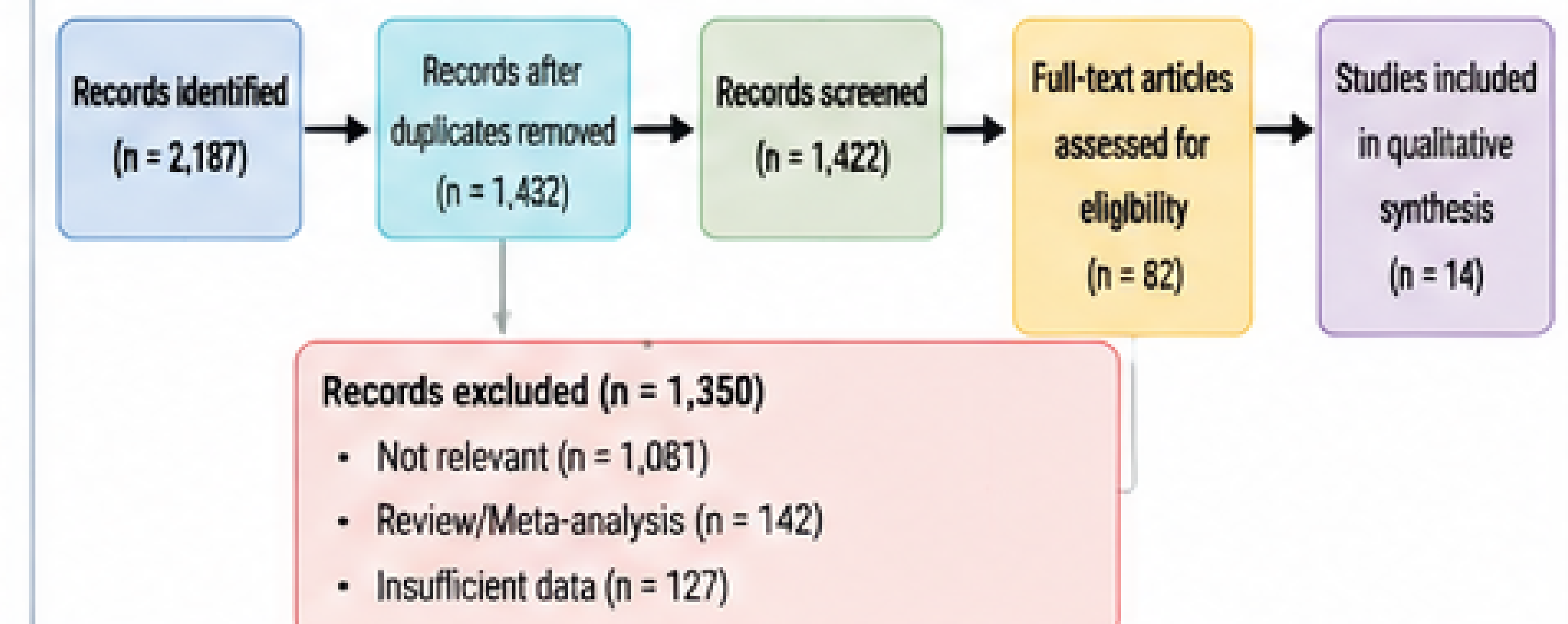


GRADE assessment indicated **very low certainty** for miRNAs and **low certainty** for circRNAs.

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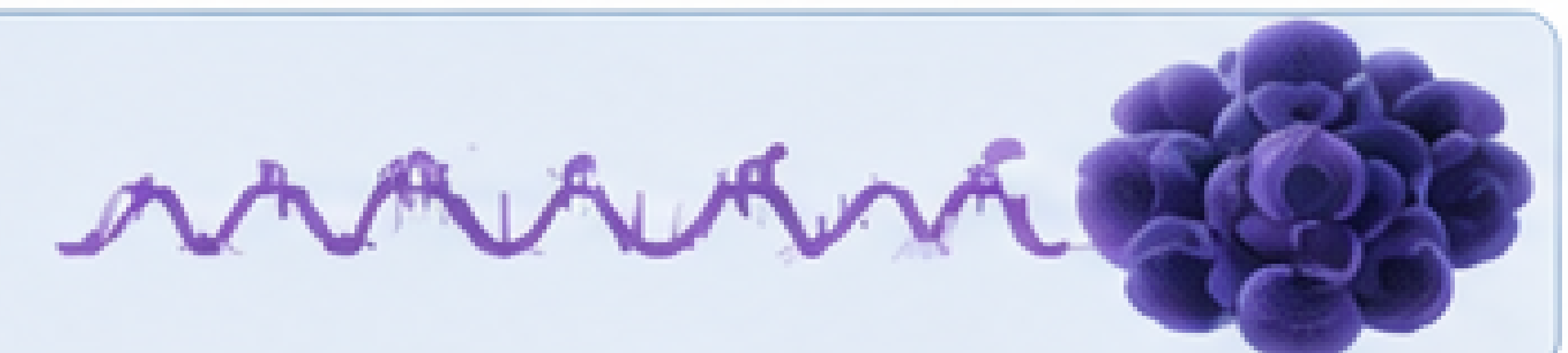


STUDY FLOW (PRISMA)



CONCLUSIONS

miRNAs demonstrate excellent diagnostic potential for CLL, whereas circRNAs show moderate accuracy. However, methodological limitations, publication bias, and small sample sizes reduce confidence in current evidence. Larger, high-quality prospective studies are required to validate ncRNAs as reliable diagnostic biomarkers in CLL.



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