# Differential Expression, Diagnostic and Prognostic Accuracy of Micrornas in Oral Cancer: An Umbrella Review and Updated Systematic Review with Meta-Analysis

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## Abstract

**Background:** Oral cancer imposes a substantial global burden because most patients present late, and current tools inadequately stratify risk. MicroRNAs (miRNAs)—small, post-transcriptional gene regulators—are promising biomarkers for early detection and prognosis, but inconsistent study designs, biospecimens, and analytic pipelines have limited clinical uptake. This study synthesises the best available evidence to quantify the diagnostic accuracy, prognostic value, and directionality of dysregulation of miRNAs in oral cancer.

**Aims and Objectives:** This review aimed to investigate the potential link between miRNA dysregulation and oral cancer, explore the diagnostic capabilities of miRNAs, and evaluate their role in predicting prognostic outcome.

**Methodology:** We conducted a meta-analysis by integrating data from systematic reviews and their cited primary studies. All effect sizes were extracted or recalculated from the original studies to ensure consistency. Random-effects models were applied to all syntheses. Prognostic effects were assessed using hazard ratios (HRs) for overall and cancer-specific survival. The diagnostic performance was evaluated using the area under the receiver operating characteristic curve (AUC). Differential expression used standardised mean differences (SMDs), either directly reported or converted from fold-change, where appropriate. Heterogeneity was assessed using $I^2$ and $\tau^2$; small-study effects/publication bias with Egger's test and influence diagnostics. Prespecified subgroup analyses were performed by effect type and direction of dysregulation (oncogenic vs. tumour suppressor) and explored biospecimen differences (tissue, serum, and saliva).

**Results:** The prognostic entries demonstrated that miRNA overexpression was associated with significantly poorer survival (pooled HR 2.31, 95% CI 1.96–2.73), with no between-study heterogeneity ($I^2$=0%) once CSS HR values were included and no evidence of small-study effects or influential outliers. Twelve diagnostic studies yielded a pooled AUC of 0.787 (95% CI 0.721–0.841), indicating moderate-to-high accuracy overall; however, performance varied across non-invasive matrices, with serum and saliva showing notable inconsistencies. Eleven expression entries produced a near-null overall SMD (−0.05, 95% CI −0.19 to 0.09), but subgroup analysis revealed biologically coherent patterns: oncogenic miRNAs were upregulated (SMD +0.29), and tumour-suppressive miRNAs were downregulated (SMD 0.52), trends masked in the aggregate estimate.

**Discussion:** The findings confirm that dysregulated miRNA expression in OSCC carries robust prognostic information and that miRNA-based assays demonstrate promising diagnostic capability. The lack of heterogeneity in prognostic analyses underscores signal stability across platforms and cohorts, whereas variability in non-invasive diagnostics highlights pre-analytic and analytic