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ORIGINAL ARTICLE

Abnormally Expressed Long Non-Coding RNAs in Nasopharyngeal Carcinoma: a Meta-Analysis

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SUMMARY

Background: **Dysregulated long non-coding RNAs (lncRNAs) have been extensively explored in nasopharyngeal carcinoma (NPC) research. The current study focused on elucidating the overall diagnostic and prognostic performances of abnormally expressed lncRNAs in NPC.**
Methods: **We performed a systematic literature search based on the online databases. The pooled effects sizes for diagnosis and prognosis were synthesized using a fixed or random effect model. Hazard ratios (HRs) with 95% confidence intervals (CIs) for primary endpoints of overall survival (OS) and disease-free survival (DFS) were aggregated. Effects of publication bias on overall pooled accuracy were assessed via trim and fill adjustment method.**
Results: **Thirteen studies comprising 580 cases for diagnosis and 1,400 for prognosis were included. The results showed that abnormally expressed lncRNAs could distinguish NPC from non-cancerous individuals with a pooled sensitivity of 0.65 (95% CI: 0.63 - 0.68), specificity of 0.83 (95% CI: 0.80 - 0.86), and AUC (area under the curve) of 0.79. For prognosis, abnormally expressed lncRNAs (high vs. low) were associated with worse survival times in both OS (HR = 2.88, 95% CI: 1.97 - 4.21, p = 0.000) and DFS (HR = 2.13, 95% CI: 1.56 - 2.90, p = 0.000) in NPC patients. Moreover, stratified analyses manifested that lncRNA transcription level was markedly correlated with TNM classification, clinical stage, and distant metastasis.**
Conclusions: **Our data evidence that abnormally expressed lncRNAs may be rated as promising biomarkers or indicators for cancer diagnosis and prognosis in NPC.**
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Supplementary Tables and Figures.

Table 1. Study quality of the diagnostic studies judged by QUADAS checklist (14-items).

Study	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Item 12	Item 13	Item 14
Zhang 2013	1	1	0	1	1	1	1	1	0	1	1	1	0	0
Gao 2014	1	1	1	1	1	1	1	1	0	1	1	1	0	0
Song 2016	1	1	1	1	1	1	1	1	0	1	1	1	0	0
He 2017	1	1	1	1	1	1	1	1	0	1	1	1	0	0

Item 1: Representative spectrum? Item 2: Acceptable selection criteria? Item 3: Acceptable reference standard? Item 4: Short time period between tests? Item 5: All participants received reference standard? Item 6: Same reference criteria used? Item 7: Reference criteria independent of Index test? Item 8: Repeatability of the Index test? Item 9: Repeatability of reference criteria? Item 10: Blinding of researchers to reference? Item 11: Blinding of researchers to index test? Item 12: Availability of clinical data? Item 13: Uninterpretable results reported? Item 14: Withdrawals explained?.

Table 2. Evaluation of the bias from retrospective cohort studies by the NOS checklist.

Study	Selection (total scores: 4)				Comparability (total scores: 2)	Outcome measurement (total scores: 3)		
	Representa-tiveness of cases	Controls selection	Exposure definition	Endpoint definition	Comparability of cases and controls on design or analysis	Outcomes evaluation	Whether follow-up time is adequate	Follow-up time for cases and controls
Yang 2017 [20]	1	1	1	1	2	0	1	0
Guo 2017 [14]	1	1	1	1	1	0	1	0
Song 2016 [17]	1	1	1	1	1	0	1	0
Zou 2016 [23]	1	1	1	1	1	1	1	1
Song 2016 [16]	1	1	1	1	2	0	1	0
Zhang 2015 [22]	1	1	1	1	1	0	1	1
Bo 2015 [12]	1	1	1	1	1	0	1	1
Nie 2013 [15]	1	1	1	1	1	1	1	1
Tang 2017 [19]	1	1	1	1	2	0	1	0
Sun 2015 [18]	1	1	1	1	1	0	1	1
Zhang 2013 [21]	1	1	1	1	2	0	1	0

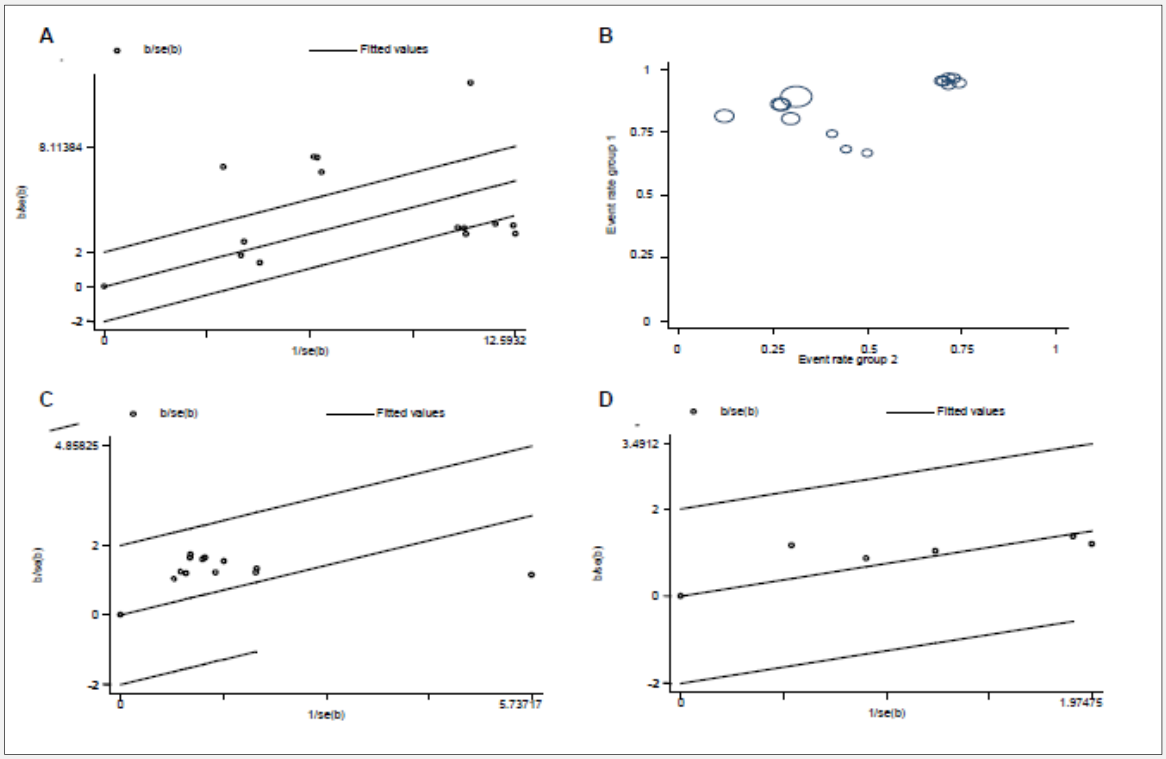

Figure 1. Heterogeneity analysis by L'Abbe and Galbraith plots.

(A) L'Abbe plot and (B) Galbraith plot for diagnostic effect size; and (C) L'Abbe plots for pooled effect sizes of OS and (D) DFS.

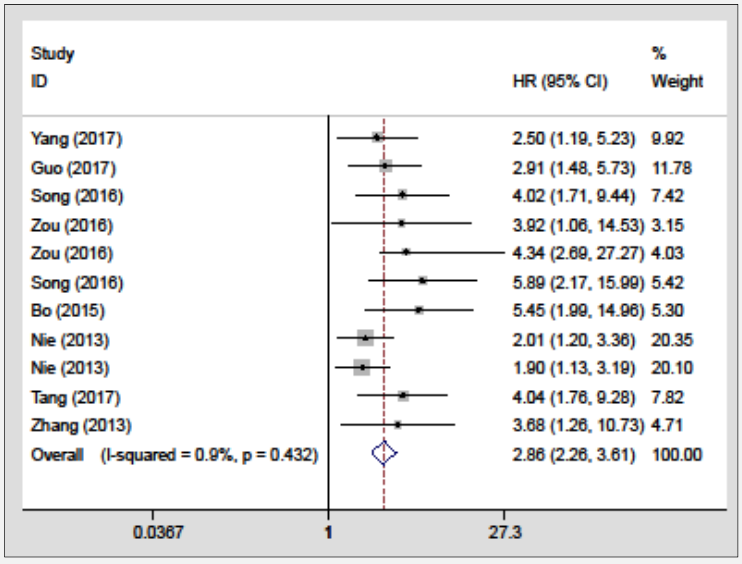

Figure 2. The pooled HR with 95%CI for OS after the outlier studies were excluded.

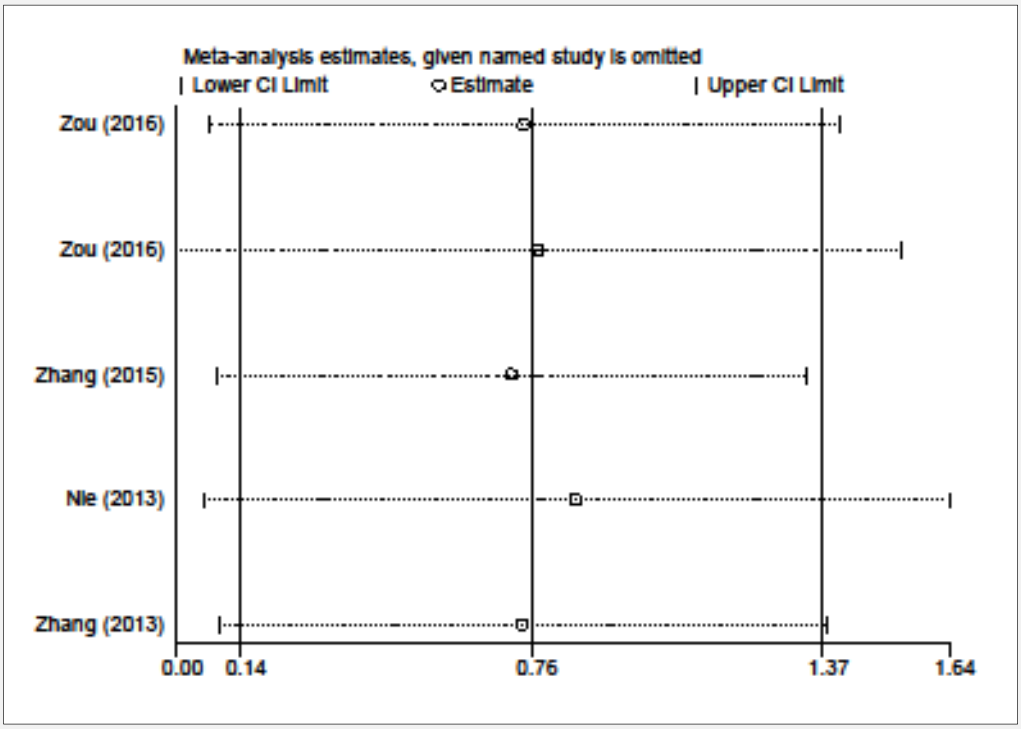

Figure 3. Sensitivity analysis of outlier studies for the prognostic meta-analysis of DFS.

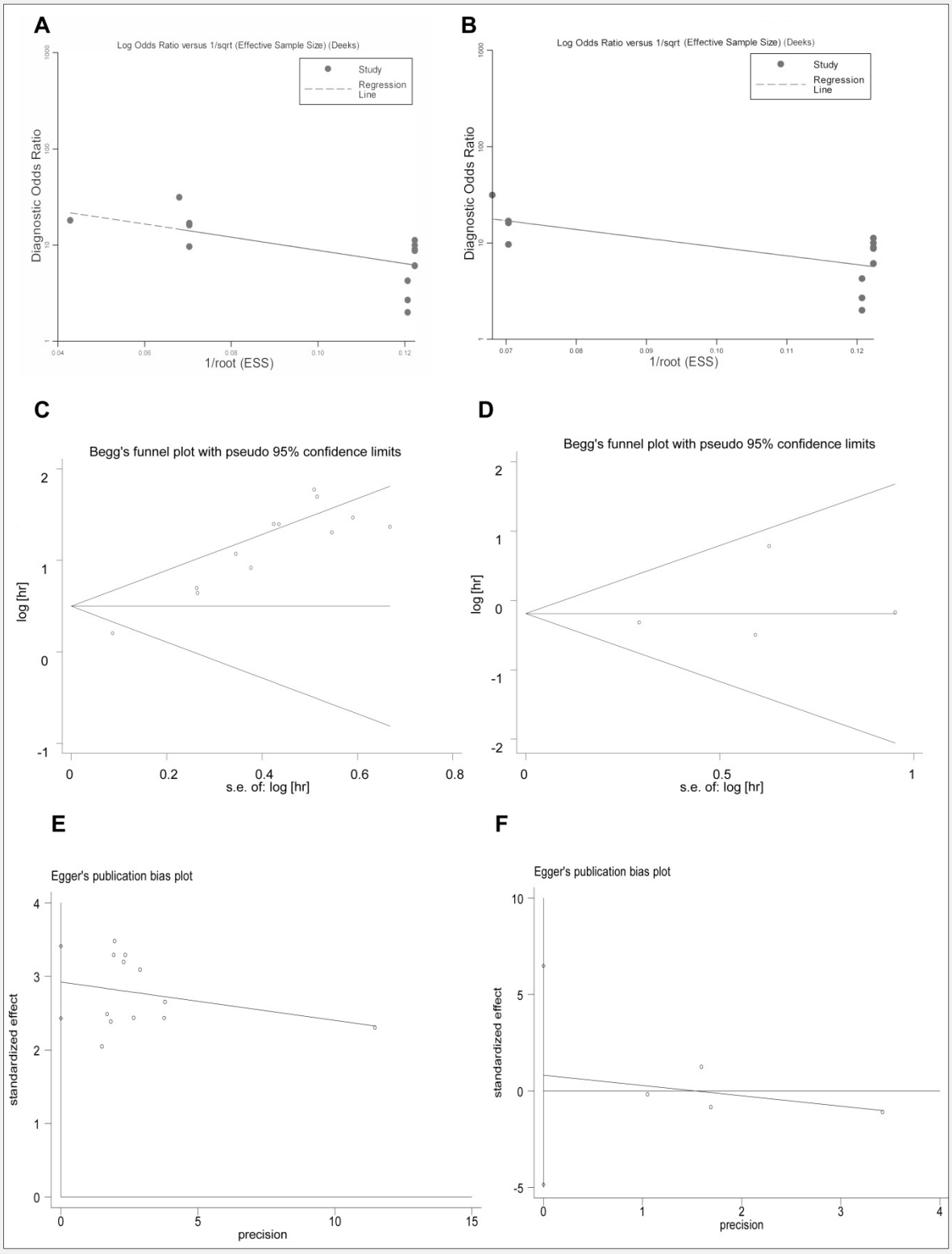

Figure 4. Publication bias analysis for the pooled analyses.

Deek's funnel plot asymmetry test for overall diagnostic meta-analysis (A) (p = 0.003) and diagnostic effect size after outlier elimination (B) (p = 0.004); Begg's test for the prognostic meta-analysis of OS (C) and DFS (D); Egger's test for the prognostic meta-analysis of OS (E)and DFS (F).