

## Peer Review File

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### Review comments:

**Comment 1:** This study is based on the analysis and summary of the literatures. It is suggested to add clinical experimental research, which may be more meaningful.

**Reply 1:** We are grateful for the suggestion. In order to make the review and analysis more clinical significance and reference value, we have added a more detailed discussion on HOTAIR-related HNSCC clinical experimental research. We have explained that these biomarkers can be used to monitor disease exacerbation, and help to choose treatment methods clinically.

**Changes in the text:** We have modified our text as advised (see Page 19, line 404-418).

**Comment 2:** In addition to lncRNA HOTAIR, what other lncRNAs play an important role in head and neck squamous cell carcinoma? It is recommended to add relevant content to the discussion.

**Reply 2:** We deeply appreciate the reviewer's suggestion. As suggested by reviewer, we have added the suggested content to the manuscript. We supplement and explain the role of MALAT1, UCA1 and MEG3, which are representative in head and neck squamous cell carcinoma.

**Changes in the text:** We have modified our text as advised (see Page 18, line 391-Page 19, line 403 ).

**Comment 3:** There are many databases. Why did the author only select several databases in this study for searching? Please explain the reason.

**Reply 3:** We are extremely grateful to reviewer for pointing out this problem. The research was implemented in the following online databases: PUBMED, Web of Science, Embase, Cochrane Library and SCOPUS. Referring to previous studies, these databases are most commonly used in cancer-related meta-analysis. We try to achieve

a comprehensive search, but in order to maintain the same or more stringent inclusion criteria as the previous meta-analysis of the same type, we also included only articles in English, but did not retrieve the Chinese database, which is also to avoid bias.

**Comment 4:** The introduction part of this paper is not comprehensive enough, and the similar papers have not been cited, such as “Effects of long noncoding RNA on prognosis of oral squamous cell carcinoma: A protocol for systematic review and meta analysis, *Medicine (Baltimore)*, PMID: 33879685”. It is recommended to quote this article.

**Reply 4:** Thank you for your careful review. We cited the articles in the introduction. In view of your suggestion, we have carefully reviewed the relevant literature and added several references to make a more comprehensive description of the role of lncRNAs in HNSCC.

**Changes in the text:** We have modified our text as advised (see Page 3, line 59-65).

**Comment 5:** There have been many studies on head and neck squamous cell carcinoma. What is the difference between this study and previous studies? What is the innovation? These need to be described in the introduction.

**Reply 5:** Thank you for your comment, and our reply is as follows: With regard to the difference from previous articles and the content of the innovative part, we have previously placed it in the discussion section. Now, we have adjusted this content to the introduction. In the previous article, the number of included studies is too small and the heterogeneity was not explained, so the reliability and accuracy of the results are insufficient. Our meta-analysis included more samples. The inclusion criteria are more strict and the outcome indicators are more comprehensive. Moreover, we test heterogeneity through sensitivity analysis and subgroup analysis, and obtain more accurate and reliable conclusions after excluding outliers.

**Changes in the text:** We have modified our text as advised (see Page4, line 83- Page5, line 106).

**Comment 6:** To further define the role of lncRNA HOTAIR in head and neck squamous cell carcinoma, larger multicenter clinical cases are needed.

**Reply 6:** Thank you for your comments. Although compared with the previous meta-analysis of the same topic, the sample size of this research increased a lot, the number of studies included is still insufficient, and most studies are conducted in China. Hence further large-scale studies should be conducted among different ethnic groups. In the future, we will continue to focus on this research. When more studies that meet the requirements can be included, we will update this meta-analysis.