

Peer Review File

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Reviewer comments:

Abstract:

Comment 1: Line 25: “uncertainties” please clarify

Reply 1: What we mean is that there are many treatment options for head and neck cancer, including surgical treatment, chemotherapy, radiotherapy, targeted therapy and immunotherapy. We have modified our text as advised (see Page 2, line 25).

Changes in the text: Head and neck cancer (HNC) comprises a heterogeneous group of cancers. In view of the distinct biological characteristics and uncertainties regarding treatment strategies, clinical physicians require high-quality clinical practice guidelines (CPGs) which could provide reliable recommendations on medical practices.

Comment 2: Line 30 “Wanfang” please explain what that is

Reply 2: Wanfang Data is an extensive database of Chinese scientific and technical information, similar to Medline and CNKI.

Comment 3: In the “methods” please add more information about number of possible articles to include, inclusion and exclusion criteria.

Reply 3: We added some data (see Page 2, line 29,30 and 32-34).

Changes in the text: We developed rigorous search strategies before searching the domestic and international literature databases (n=568) including Medline (via PubMed), Chinese National Knowledge Infrastructure (CNKI) and Wanfang as well as websites of guideline organizations (n=8) from January 2018 to July 2021 published between January 1, 2018 to July 1, 2021. We included all evidence-based guidelines about HNC in English or Chinese. We excluded translations, summaries and interpretations of guidelines, as well as older versions of guidelines if an updated edition was available.

Comment 4: It is unclear what you mean with “searching... from January 2018 to July 2021”.

Reply 4: We included all evidence-based guidelines on CRC published between January 1, 2018 to July 1, 2021. We have revised the statement to make it clearer (see Page 2, line 31).

Changes in the text: We developed rigorous search strategies before searching the domestic and international literature databases (n=568) including Medline (via PubMed), Chinese National Knowledge Infrastructure (CNKI) and Wanfang as well as websites of guideline organizations (n=8) from January 2018 to July 2021 published between January 1, 2018 to July 1, 2021.

Comment 5: Please expand the results reported here.

Reply 5: We added some data (see Page 2, line 38-41).

Changes in the text: The proportions of reported items in each RIGHT domain were 75.4% for Basic information, 63.1% for Background, 42.9% for Evidence, 55.1% for Recommendations, 42.9% for Review and quality assurance, 26.2% for Funding and declaration and management of interests, and 50.8% for Other information.

Comment 6: Conclusion: it would be valuable if the authors could add a sentence about what they think about their results.

Reply 6: We added some data (see Page 2, line 43-44).

Changes in the text: Our research would help optimize the development processes of guidelines, resulting in high-quality guidelines for healthcare professionals.

Introduction:

Comment 7: Line 47: “unpredictable manifestations and outcomes”- please clarify

Reply 7: Because HNC includes a group of diseases, and there are many different anatomical locations of origin. This leads to a lot of clinical manifestations. For example, common clinical symptoms of nasopharyngeal carcinoma include nasal congestion, blood in the nasal discharge, and hearing loss. Common clinical symptoms of throat cancer include hoarseness and sore throat. We have revised the statement to make it clearer (see Page 3, line 53).

Changes in the text: Together with the different anatomical locations of origin, these lead to different manifestations and outcomes.

Comment 8: Please include more information about standard treatments for HN cancer.

Reply 8: We added some data (see Page 3, line 59-64).

Changes in the text: In general, patients with early-stage HNC are treated with surgery or radiotherapy as a single modality and have favorable outcomes. However, locally advanced diseases at diagnosis usually require multi-modality therapies. Palliative chemotherapy is the treatment for most recurrent and/or metastatic HNC. Immune checkpoint inhibitors have been rapidly developed in the treatment of advanced HNC in recent years. Many clinical trials are exploring the possibility of combining immunotherapy with other treatment modalities.

Comment 9: Line 54: Is there some text missing here? “... prognosis of HNC also have many indicators”, please clarify.

Reply 9: We added some data (see Page 3, line 66 and page 4, line67-69).

Changes in the text: Previous studies have shown that increased infiltration of CD3⁺, CD8⁺, CD4⁺ and Foxp3⁺ tumor-infiltrating lymphocytes (TILs) are associated with better prognosis in HNC. High CD4⁺ and CD8⁺ TIL were significantly associated with improved OS in oropharyngeal cancer, and high CD8⁺ was significantly associated with improved OS in hypopharyngeal cancer.

Material and methods:

Comment 10: There are many kinds of guidelines for HN cancer patients, before starting cancer treatment, what should be done during treatment (i.e visits to different health care

professionals, medications to treat symptoms and pain due to treatment), what should be done after completed treatment (follow-ups, rehabilitation, continued contact with health care professionals). Please include information about if all or just a few of these were included. It is my experience that health care has their guidelines and dentistry has their. Were guidelines regarding oral and dental care in connection with HN cancer treatment included?

Reply 10: Sub-items 1c was about the focus of the guideline description, including screening, diagnosis, treatment, management, prevention or others. Its reporting rate was above 90.5%. Head and neck cancer (HNC) comprises a heterogeneous group of cancers, including cancer of the Oral Cavity. It was included in our search strategy and selected literatures.

Comment 11: Line 76: “guidelines also were developed...” please clarify what you mean.

Reply 11: Generally speaking, guidelines are developed and published by medical organizations or government public health agencies such as World Health Organization (WHO), National Comprehensive Cancer Network (NCCN) and the American Society of Clinical Oncology (ASCO). Also, some guidelines will be included in the database. We searched through these databases and websites.

Comment 12: Line 85: Please write about the number of hits the searches generated here.

Reply 12: We added some data (see Page 4, line 101-102).

Changes in the text: We adjusted the format when we were searching through different databases and ended up with a total of 576 records.

Comment 13: Line 97: “investigators” who were they?

Reply 13: We added some data (see Page 6, line 113-114).

Changes in the text: Two investigators (Jiabao Hou and Xuan Wu) completed this procedure independently.

Comment 14: Line 102: “independent expert” who was that?

Reply 14: We added some data (see Page 6, line 118).

Changes in the text: Disagreement would be resolved by discussion or further recommendations from an independent expert (Qiming Wang).

Comment 15: Line 106: “all data would be checked and verified”- please clarify what you mean here

Reply 15: Our research includes the following steps: Literature search, Data collection and Data analysis. After each part is completed, we will check the information obtained to make sure they are correct and reliable.

Comment 16: Line 120: “expert adjudicator”- who was that?

Reply 16: We added some data (see Page 7, line 137).

Changes in the text: If disagreements arose, they would be resolved by discussion or asking for recommendations from an expert adjudicator (Qiming Wang).

Comment 17: Line 123: “showed the differences” do you mean calculated?

Reply 17: The RIGHT tool provides evaluators a clear, transparent and comprehensive checklist with accompanying explanations and detailed instructions. It contains 35 items grouped into seven domains: basic information, background, evidence, recommendations, review and quality assurance, funding and declaration and management of interests, and other information. Reporting rates are different among these seven domains. The mean reporting quality in the “Basic information” domain was highest (75.4%), and the reporting quality in the domain “Funding and declaration and management of interests” the lowest (26.2%).

Results:

Comment 18: Line 129: please include reasons for exclusion after reading titles and abstract

Reply 18: We added the reasons (see Page 7, line 146-147).

Changes in the text: After reviewing the remaining 569 records for titles and abstracts, we excluded 522 records because they were not guidelines or were not latest versions.

Comment 19: The authors should include more information about the guidelines found and included. How many concerned treatments of cancer in adults and how many in children? There are many kinds of guidelines for HN cancer patients, before starting cancer treatment, what should be done during treatment (i.e. visits to different health care professionals, medications to treat symptoms and pain due to treatment), what should be done after completed treatment (follow-ups, rehabilitation, continued contact with health care professionals). Please include information about if all or just a few of these were included.

Reply 19: Of the 21 guidelines included, three focused on HNC in children and the rest focused on HNC in adults. Sub-item 1c was about the focus of the guideline description, including screening, diagnosis, treatment, management, prevention or others. Its reporting rate was above 90.5%.

Comment 20: Line 136: “reporting rates”- can you please clarify

Reply 20: RIGHT checklist contains 35 items. The reporting rate means how many items are reported in one guideline.

Comment 21: 139: “developed by China” please specify what professions those involved had.

140: “developed by France” please specify what professions those involved had.

140-141. Please also specify this for India, Spain, the UK, the US and international collaborations.

Reply 21: Most of them are medical doctors who specialize in diagnosing, treating, and managing cancer.

Comment 22: Line 145. Please insert that those are mean values

Reply 22: We added some data (see Page 8, line 163).

Changes in the text: The mean value of the reporting rates for these seven domains ranged

from 26.2% to 75.4%, with the highest reporting rate for "Basic information" at 75.4% and the lowest reporting rate for "Funding and declaration and management of interests" at 26.2%.

Comment 23: Line 152. "reporting rate... rising and then falling". Please clarify by showing proportions.

Reply 23: We added some data (see Page 8, line 172-173).

Changes in the text: The reporting rates of guidelines published from 2018 to 2021 were 48.6%, 62.9%, 51.0% and 57.4%, respectively.

Discussion

Comment 24:

General comment: in this section there are a lot of new information that should be included in the Results section. For example, the section starting on line 184, about "Evidence" on line 192, and also text in the section starting on line 201.

Reply 24: We added some content (see Page 9, line 204-206, line 214-215 and page 10, line 224-225).

Changes in the text: The information of background includes brief description of the health problems, aims of the guideline and specific objectives, end-users and settings, target populations and guideline development groups.

The information of evidence includes systematic reviews, assessment of the certainty of the body of evidence.

The information of recommendations includes explanation for recommendations, evidence to decision processes.

Comment 25: Line 162. EBV- please write in full

Reply 25: We added some content (see Page 9, line 182).

Changes in the text: HNC is a highly heterogeneous group of cancers, which originates mainly in the oral cavity, nasopharynx, larynx, and salivary glands. In China, nasopharyngeal cancer is the most common, and the high incidence area is Guangdong province, which is related to Epstein-Barr virus (EBV) and genetic factors.

Comment 26: Line 163. How can complex anatomy and dense concentration of vital organs contribute to patients being at an advanced stage when diagnosed?

Reply 26: We have revised the statement to make it clearer (see Page 9, line 184).

Changes in the text: Most patients were already at an advanced stage when diagnosed, resulting in poor treatment outcomes and limited functional recovery.

Comment 27: Line 178. "very friendly" please clarify.

Reply 27: We mean that guidelines with clear and concise recommendations make work more efficient for doctors.

Comment 28: Line 224 "appropriate statistical methods". It is just mean values you have calculated?

Reply 28: The mean values can demonstrate the differences in different subgroups. Therefore, we only calculated the mean values.

Comment 29: Figure 3. Please insert a line explaining the numbers to the left.

Reply 29: We have added explanations (see Figure 3).